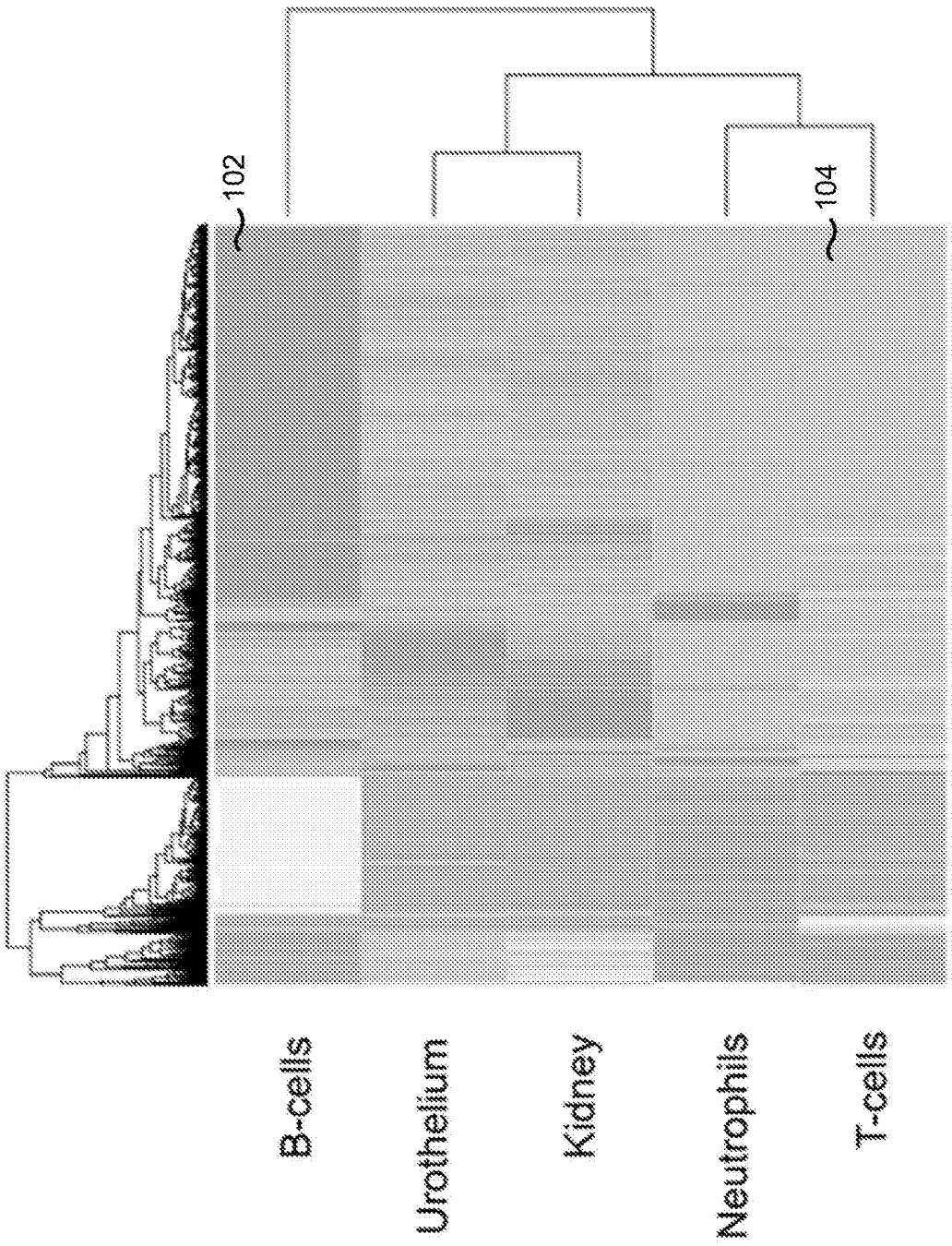


FIG. 1

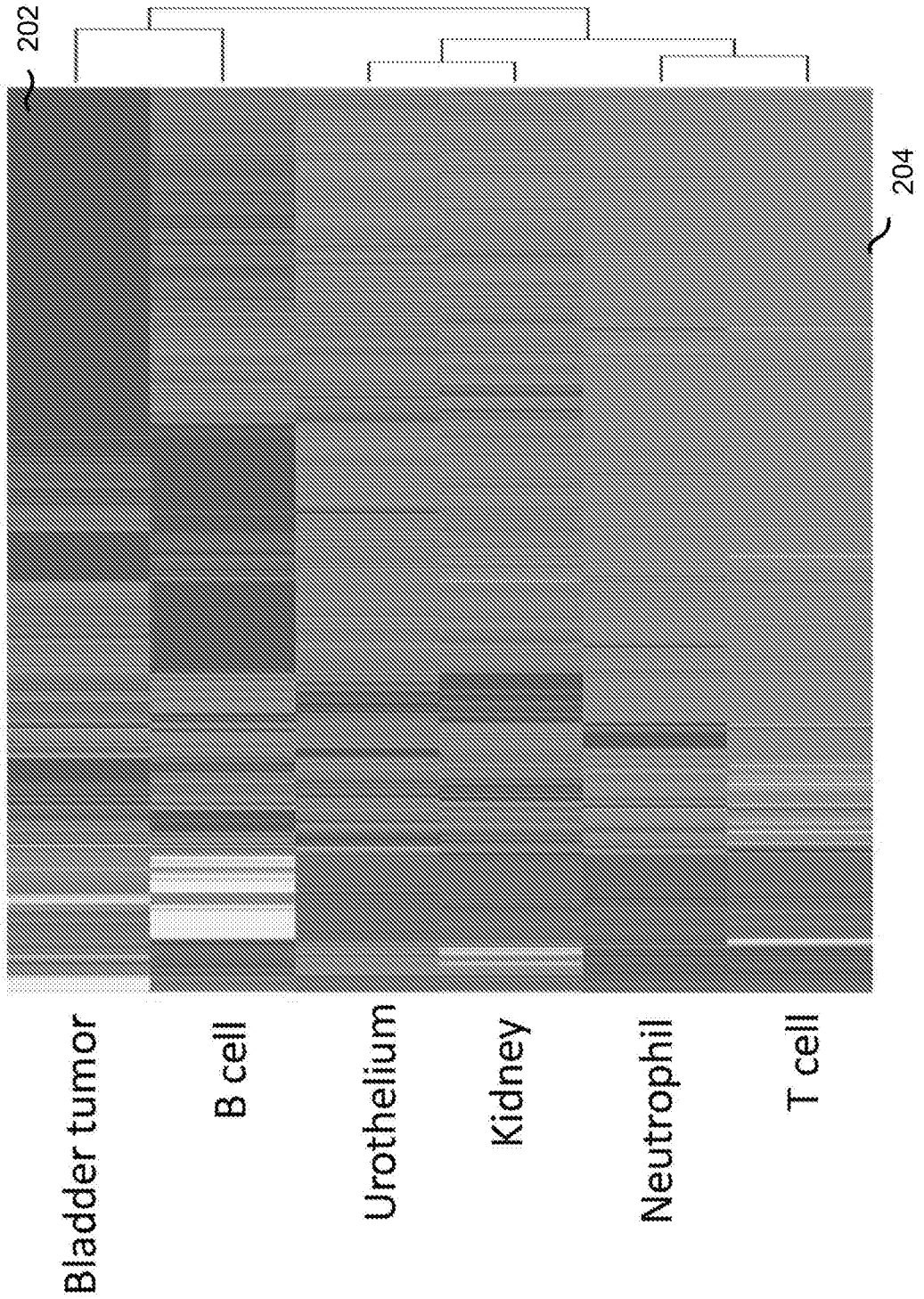

202
204
Bladder tumor
B cell
Urothelium
Kidney
Neutrophil
T cell

FIG. 2

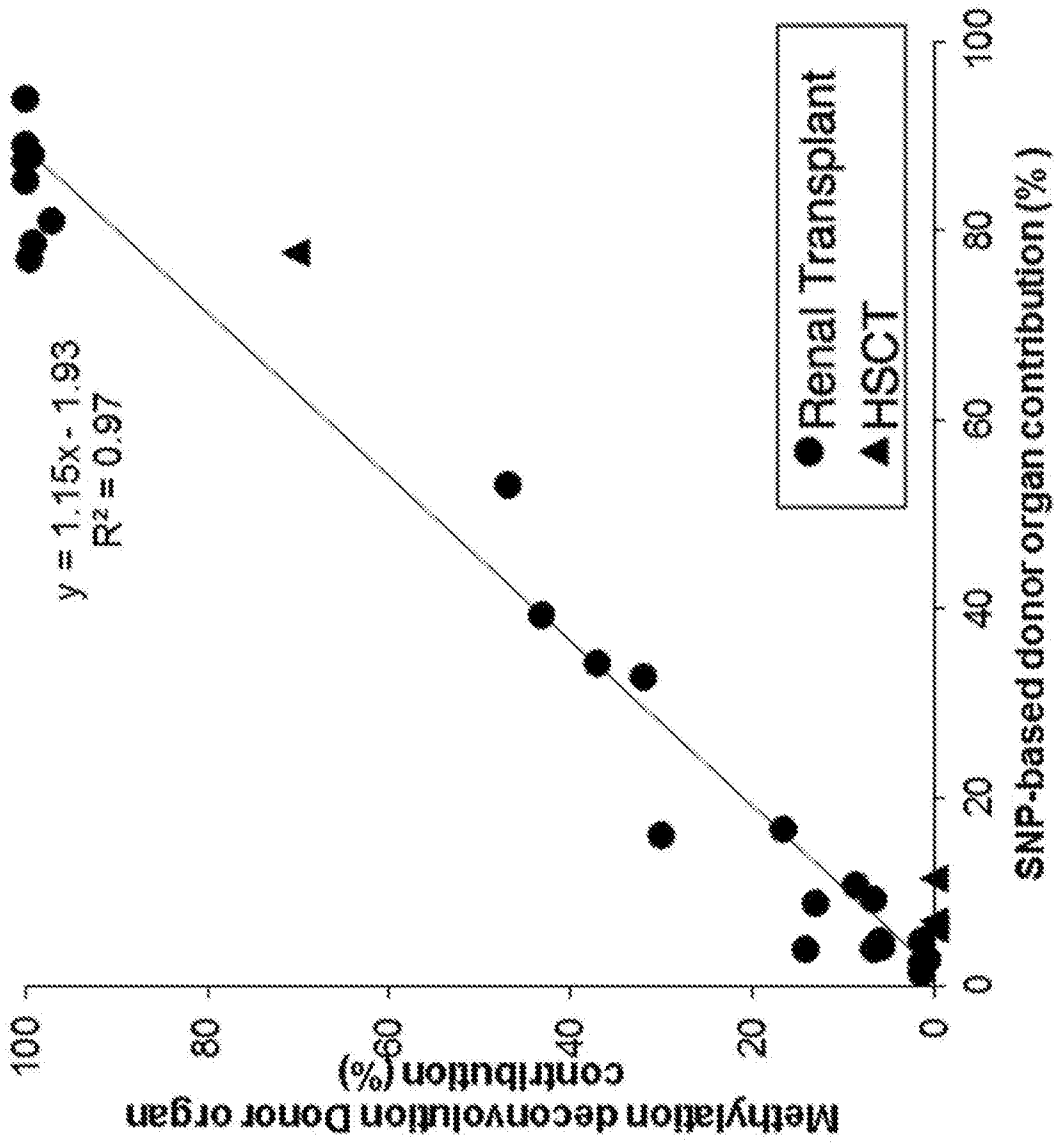

Methylation deconvolution Donor organ contribution (%)
SNP-based donor organ contribution (%)
y = 1.15x - 1.93
R² = 0.97
Renal Transplant
HSCT
0
20
40
60
80
100

FIG. 3

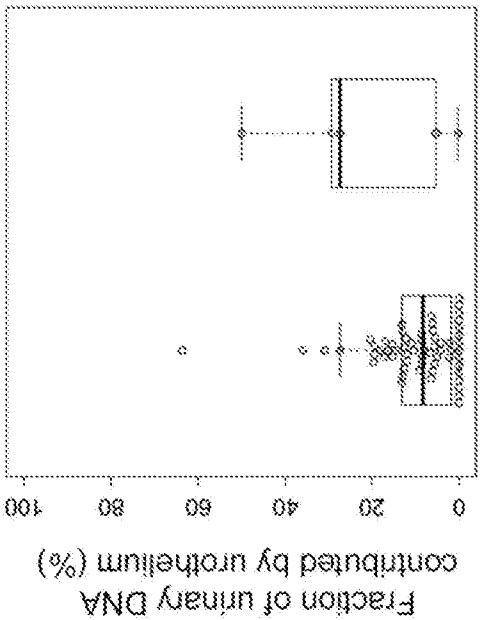


FIG. 4A

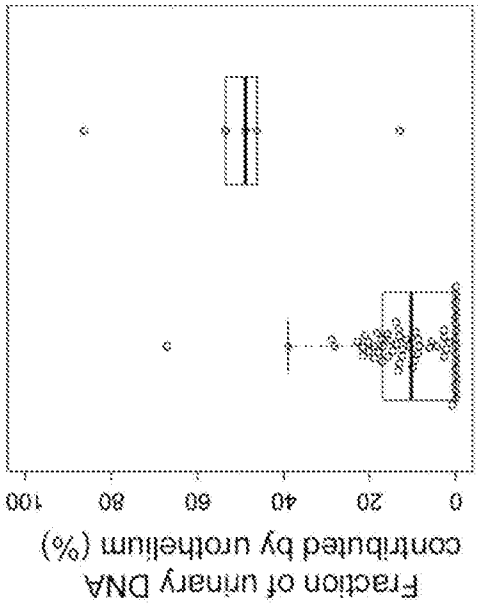


FIG. 4B

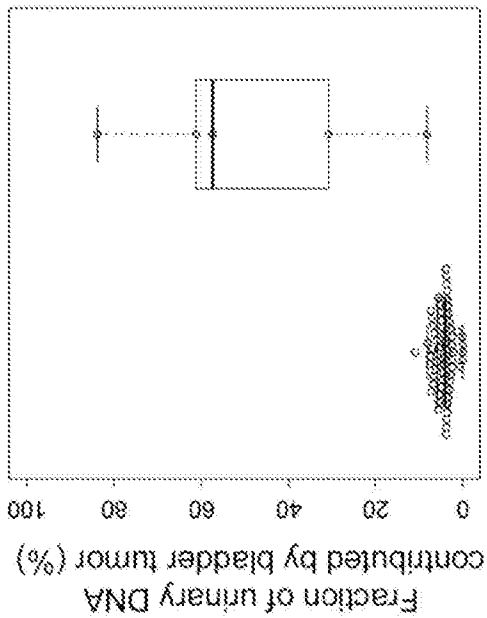


FIG. 4C

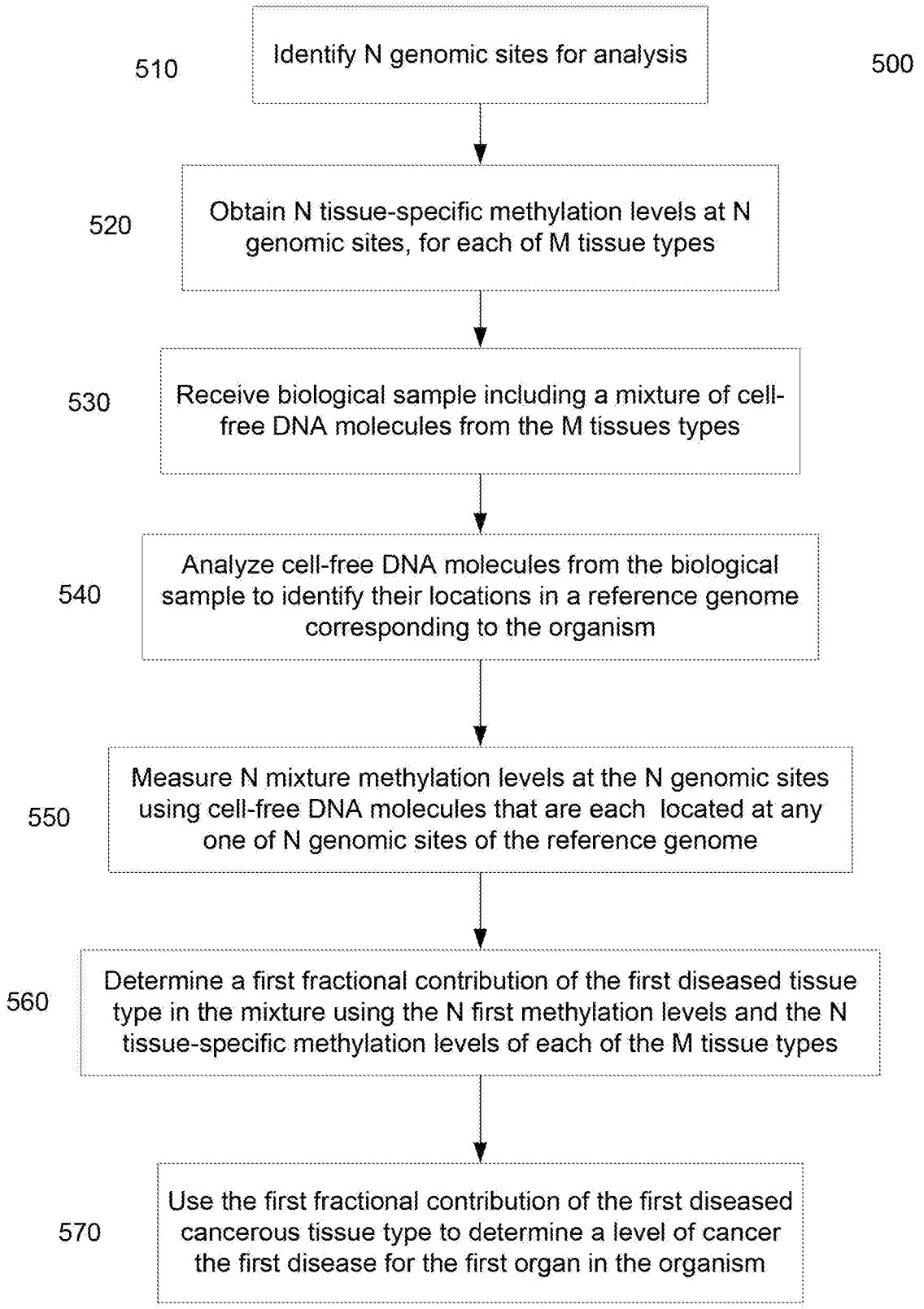

500
510
Identify N genomic sites for analysis
520
Obtain N tissue-specific methylation levels at N genomic sites, for each of M tissue types
530
Receive biological sample including a mixture of cell-free DNA molecules from the M tissues types
540
Analyze cell-free DNA molecules from the biological sample to identify their locations in a reference genome corresponding to the organism
550
Measure N mixture methylation levels at the N genomic sites using cell-free DNA molecules that are each located at any one of N genomic sites of the reference genome
560
Determine a first fractional contribution of the first diseased tissue type in the mixture using the N first methylation levels and the N tissue-specific methylation levels of each of the M tissue types
570
Use the first fractional contribution of the first diseased cancerous tissue type to determine a level of cancer the first disease for the first organ in the organism

FIG. 5

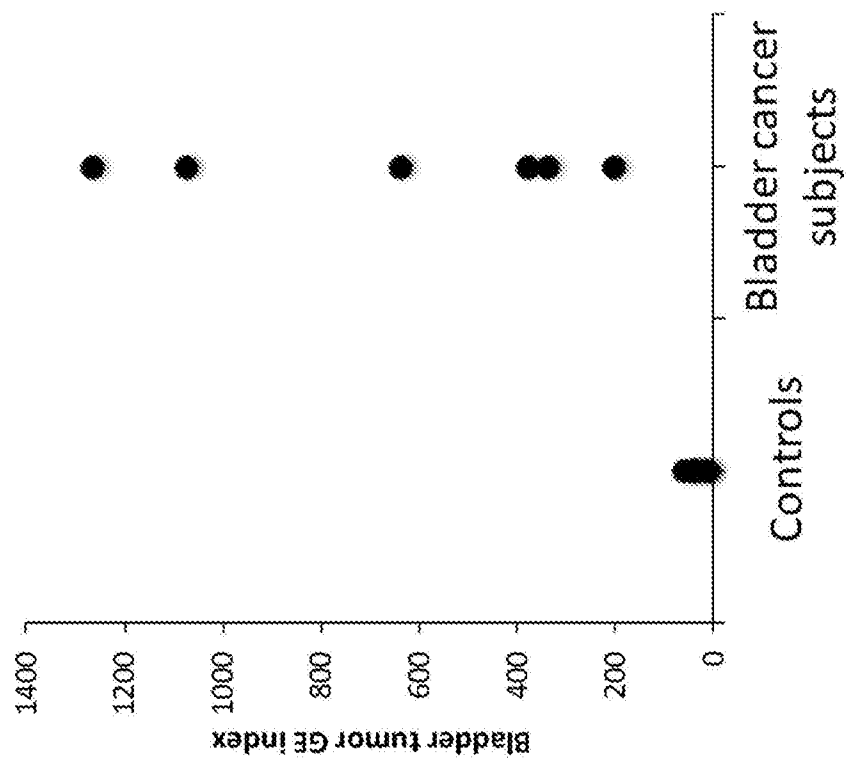

Bladder tumor GE index
1400
1200
1000
800
600
400
200
0
Controls
Bladder cancer subjects

FIG. 6B

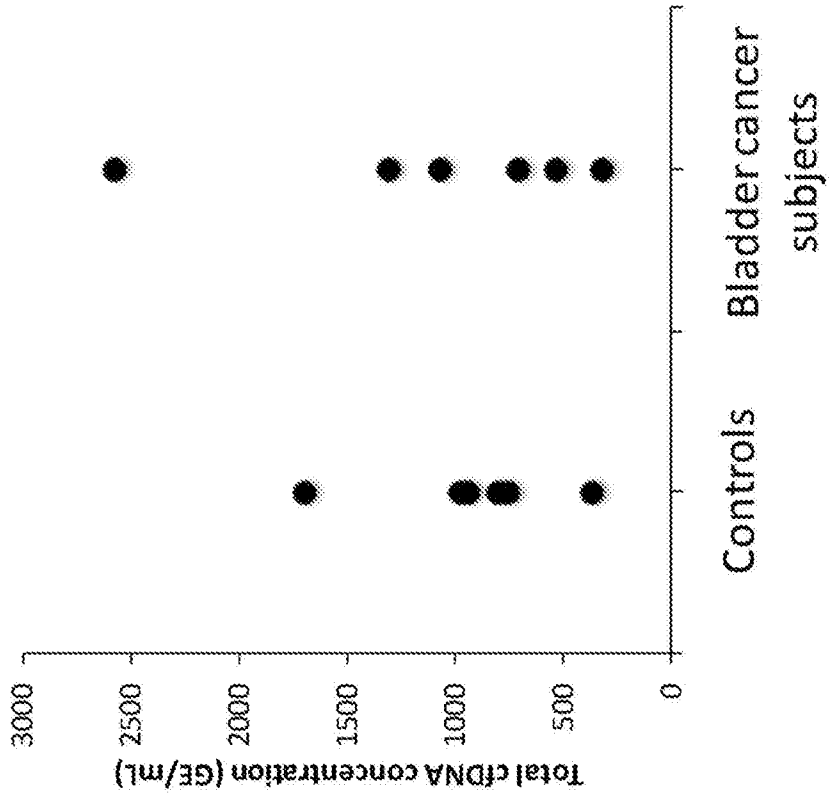

Total cfDNA concentration (GE/mL)
3000
2500
2000
1500
1000
500
0
Controls
Bladder cancer subjects

FIG. 6A

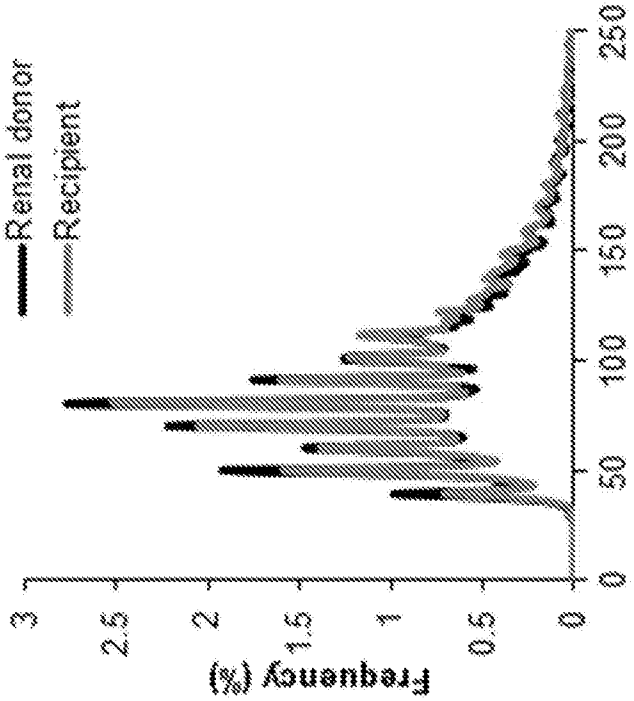

Renal donor
Recipient
Frequency (%)
Size (bp)
0
0.5
1
1.5
2
2.5
3
0
50
100
150
200
250

FIG. 7B

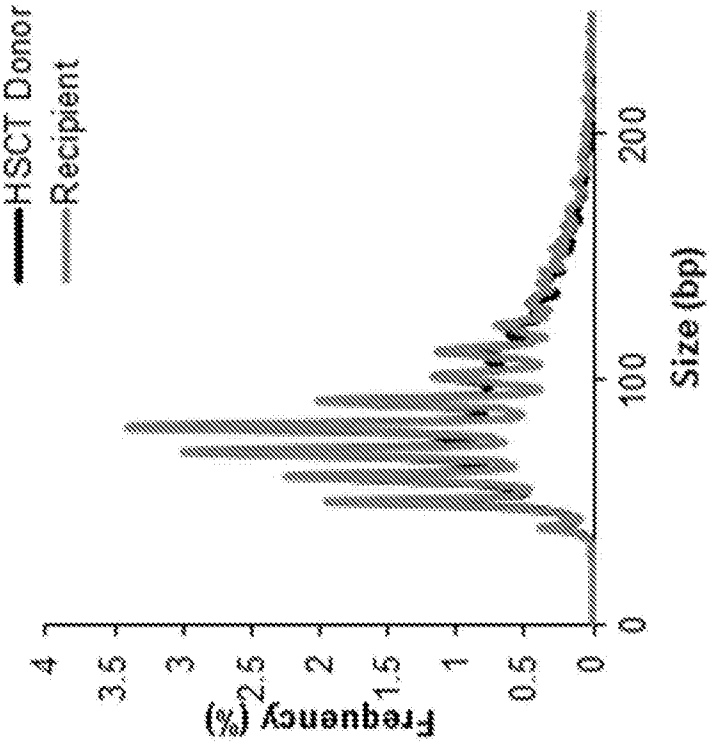

HSCT Donor
Recipient
Frequency (%)
Size (bp)
0
0.5
1
1.5
2
2.5
3
3.5
4
0
100
200

FIG. 7A

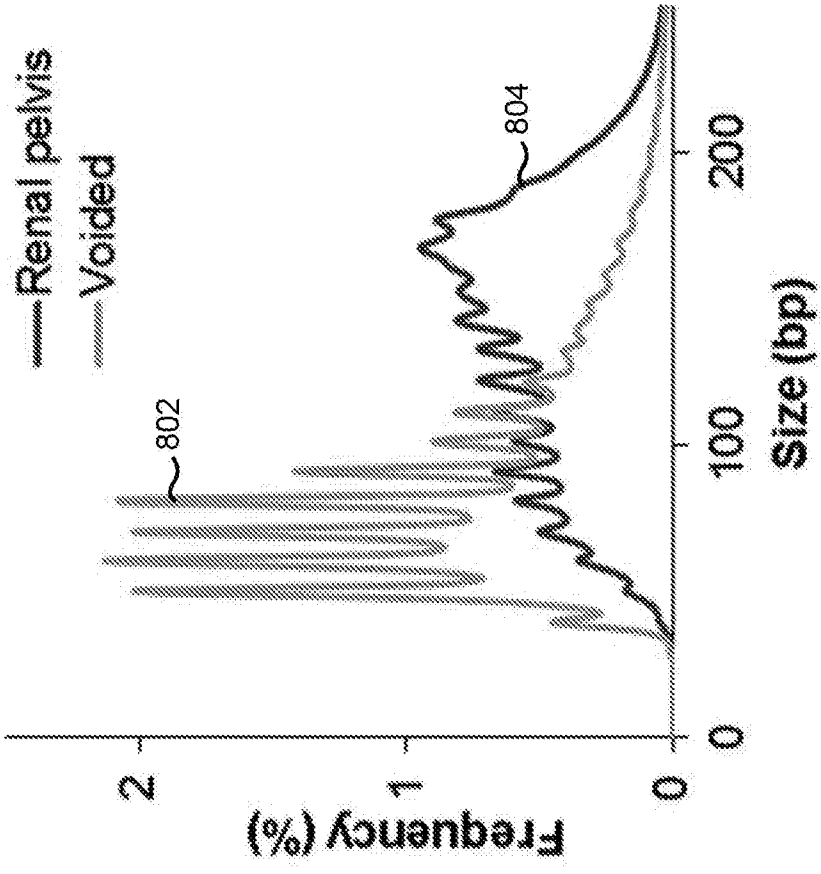

Renal pelvis
Voided
802
804
Frequency (%)
Size (bp)
0
1
2
0
100
200

FIG. 8A

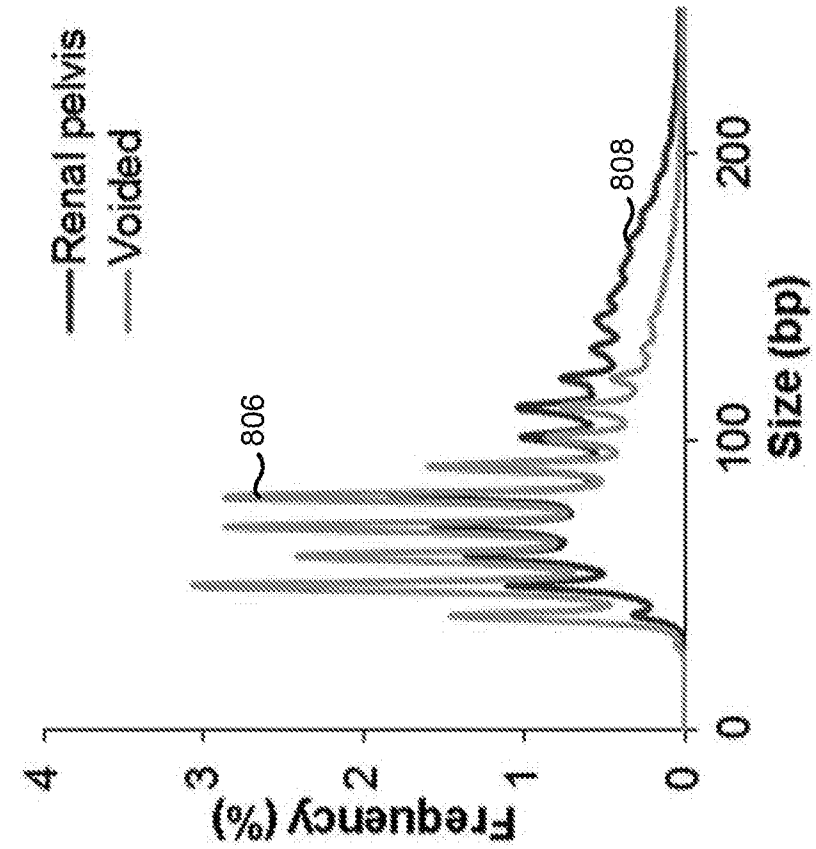

Renal pelvis
Voided
806
808
Frequency (%)
Size (bp)
0
1
2
3
4
0
100
200

FIG. 8B

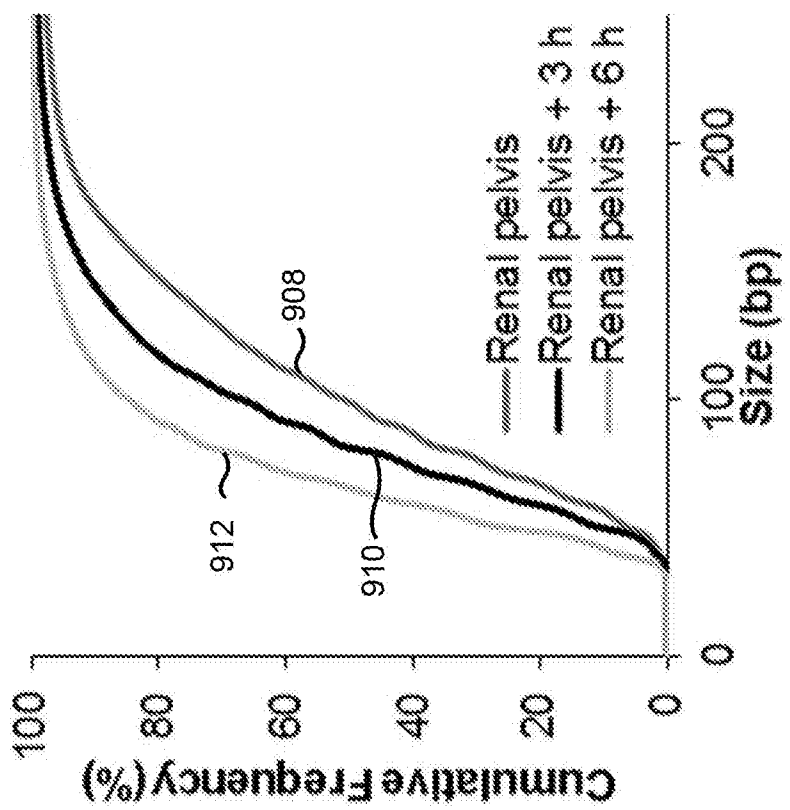

Cumulative Frequency (%)
100
80
60
40
20
0
0
100
200
Size (bp)
Renal pelvis
Renal pelvis + 3 h
Renal pelvis + 6 h
908
912
910

FIG. 9B

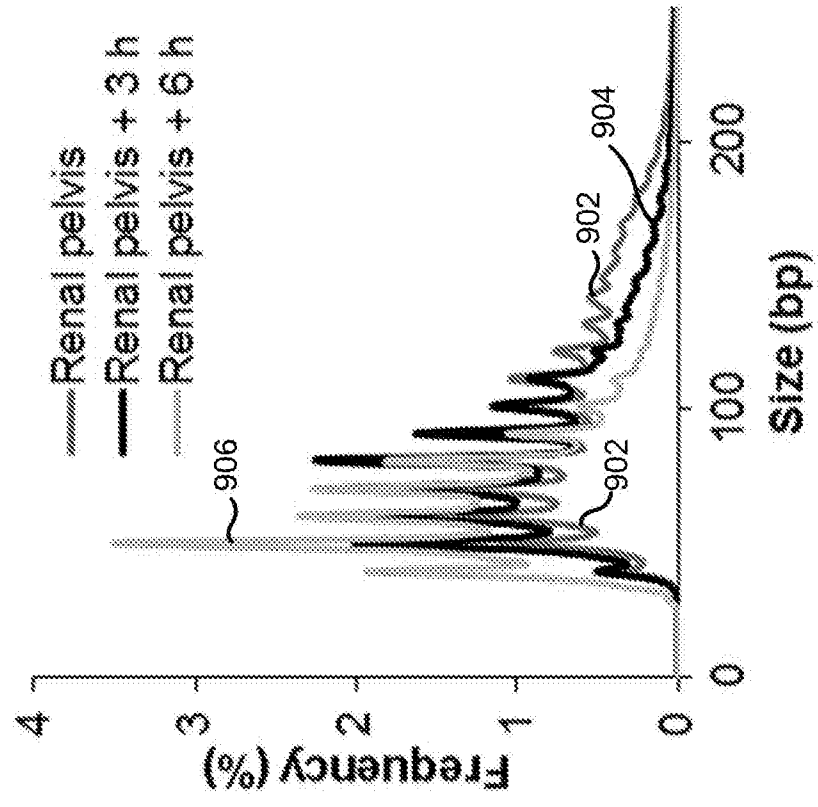

Frequency (%)
4
3
2
1
0
0
100
200
Size (bp)
Renal pelvis
Renal pelvis + 3 h
Renal pelvis + 6 h
906
902
902
904

FIG. 9A

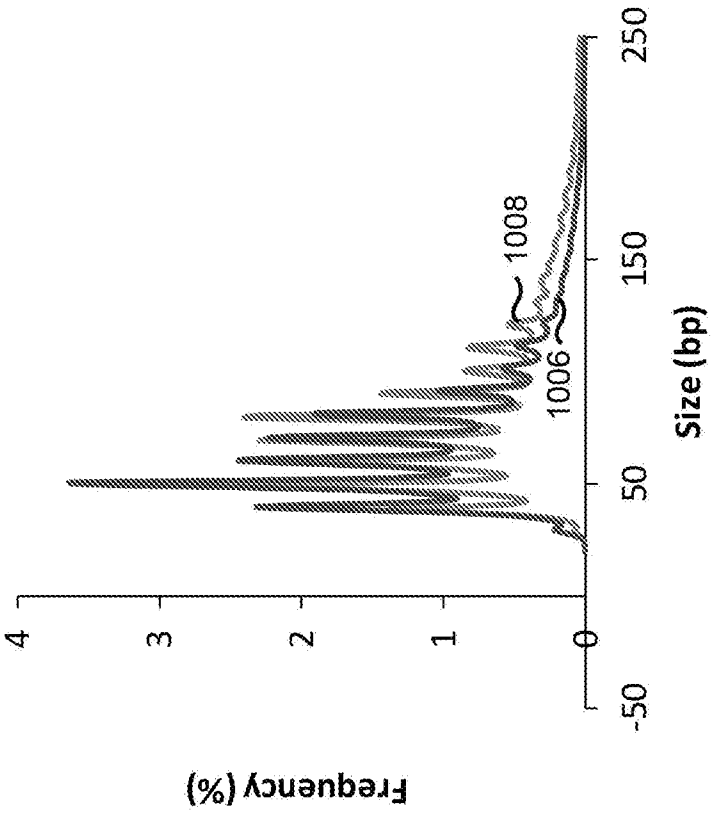


FIG. 10B

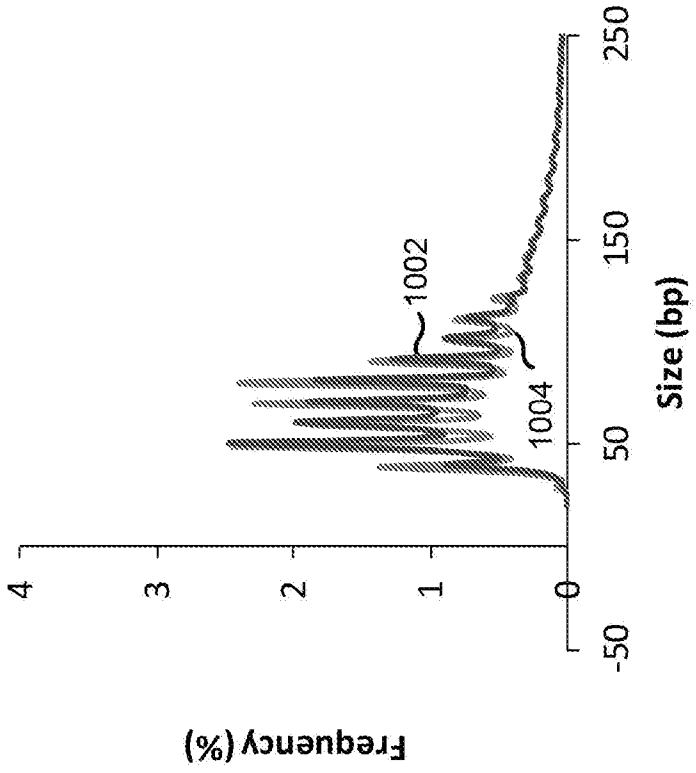


FIG. 10A

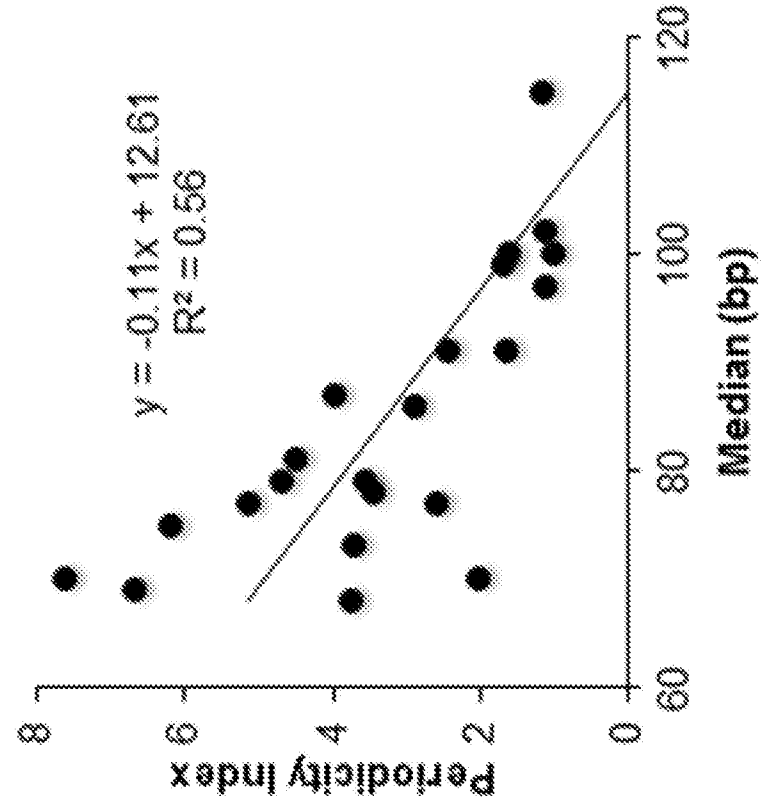


FIG. 11B

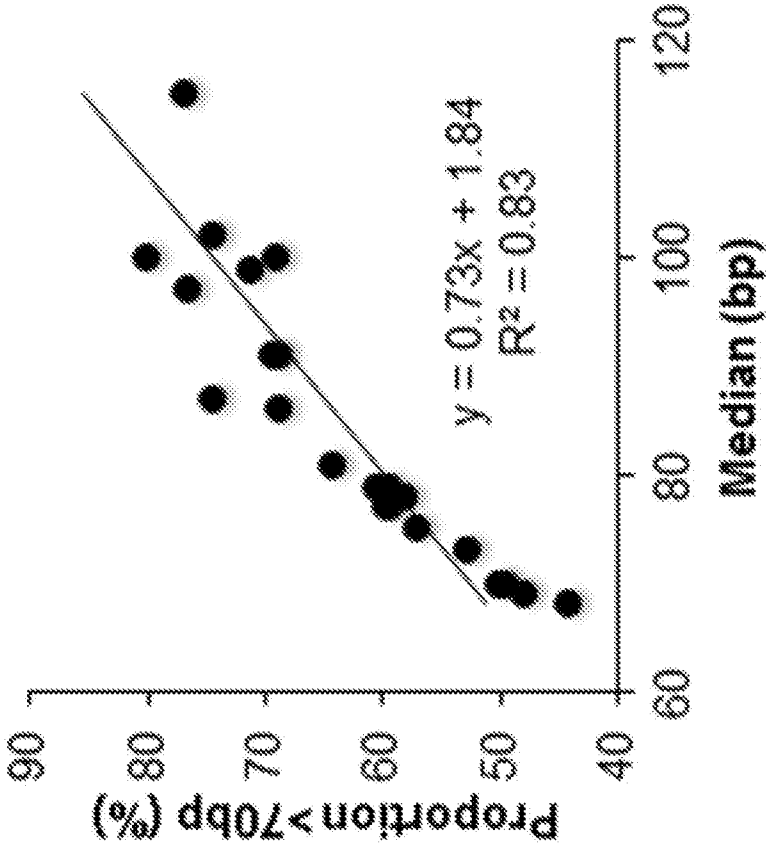


FIG. 11A

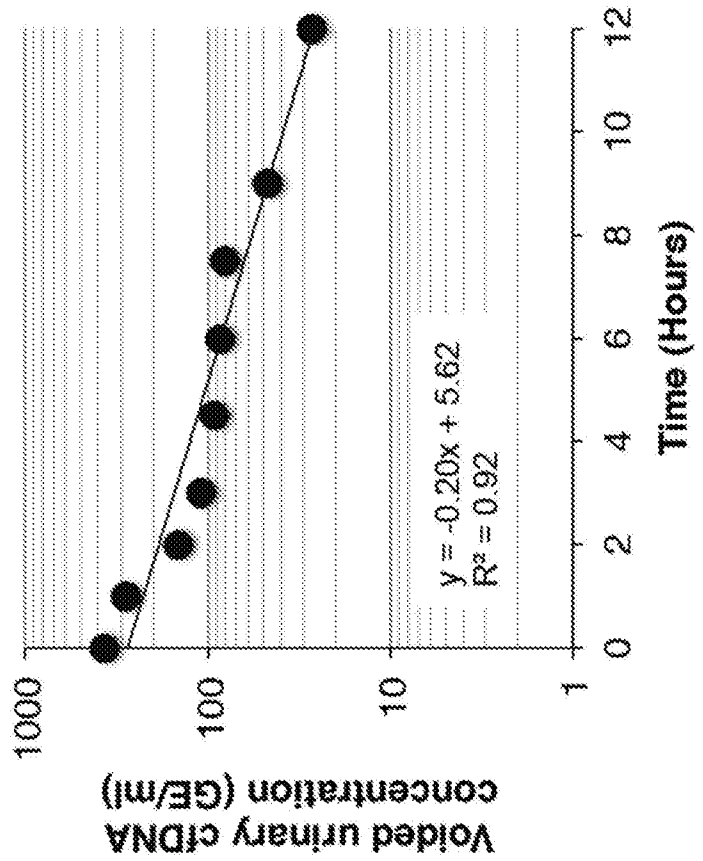


FIG. 12B

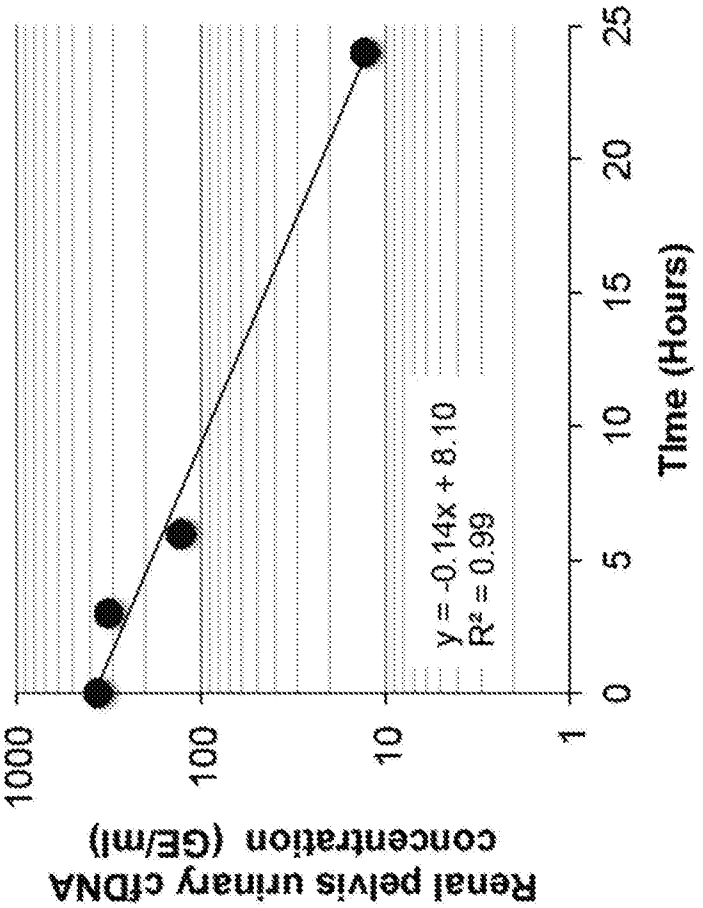


FIG. 12A

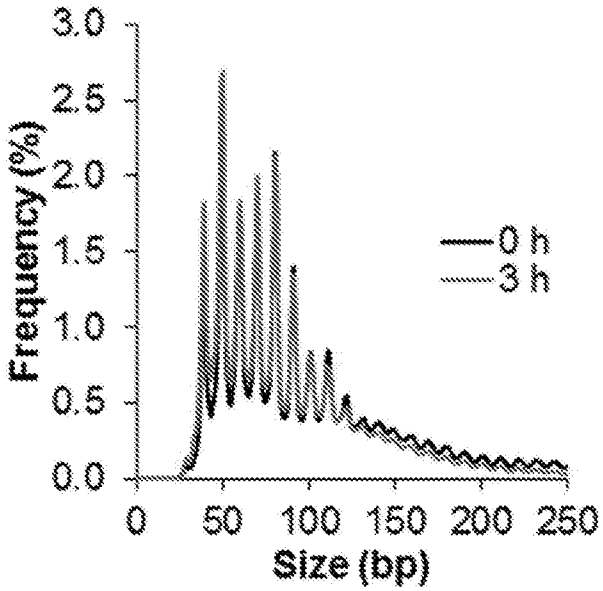


FIG. 13A

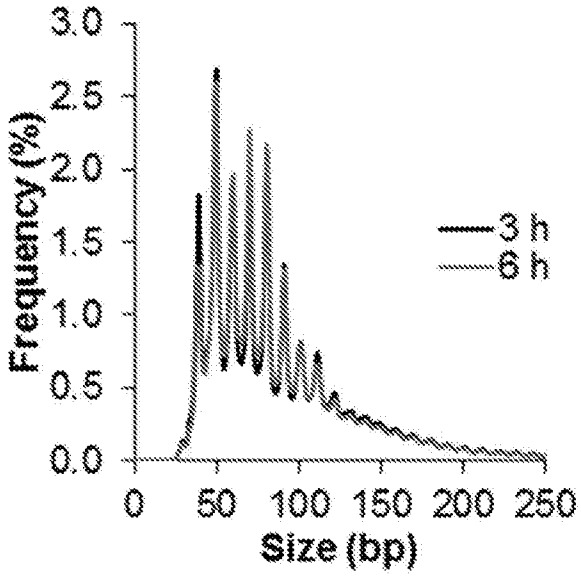


FIG. 13B

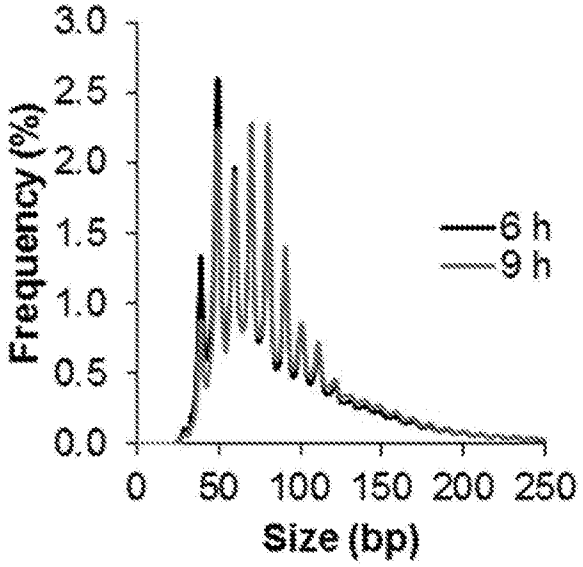


FIG. 13C

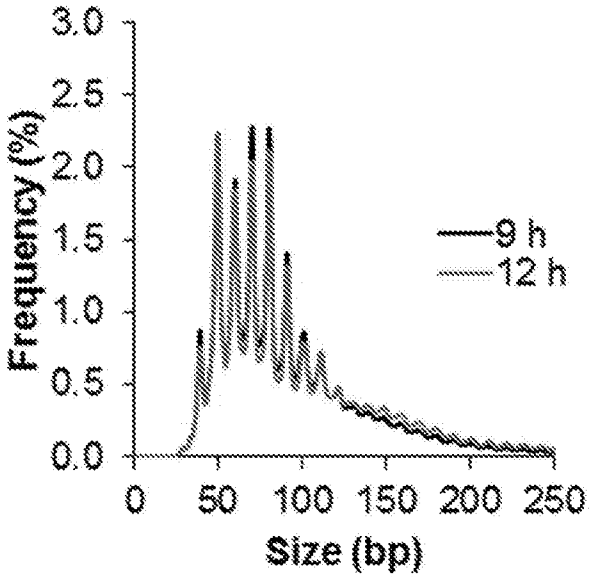


FIG. 13D

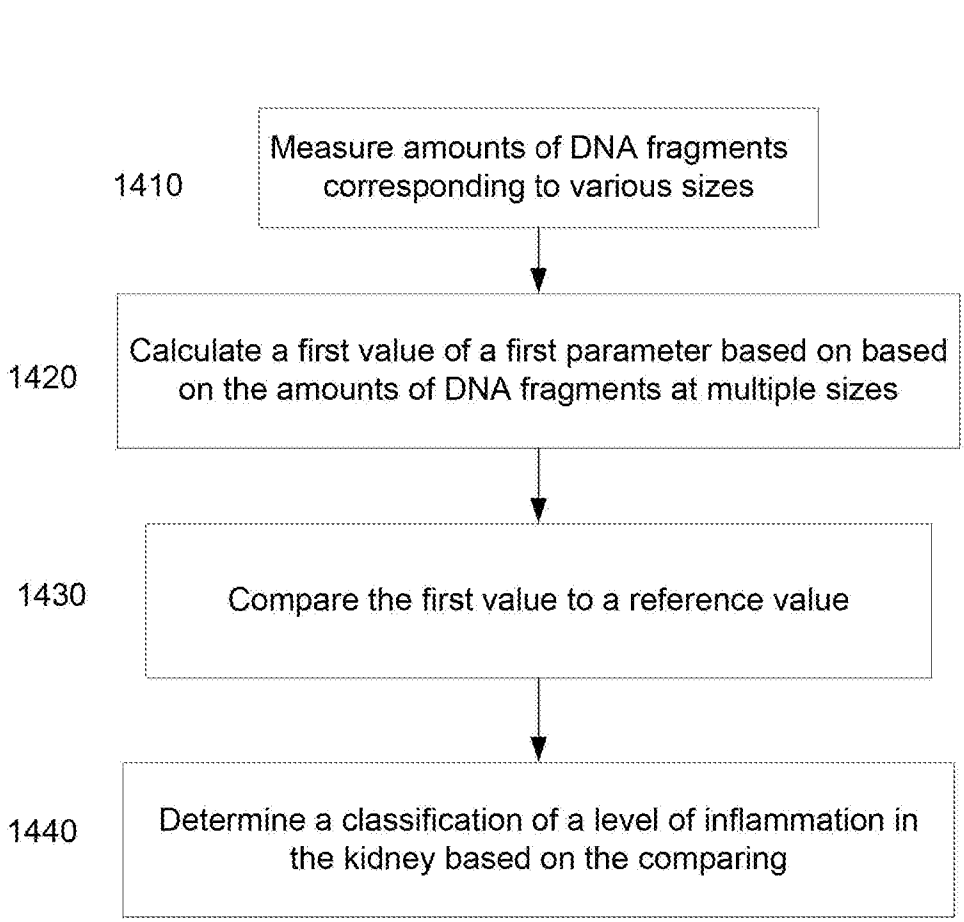

1400
1410
Measure amounts of DNA fragments corresponding to various sizes
1420
Calculate a first value of a first parameter based on based on the amounts of DNA fragments at multiple sizes
1430
Compare the first value to a reference value
1440
Determine a classification of a level of inflammation in the kidney based on the comparing

FIG. 14

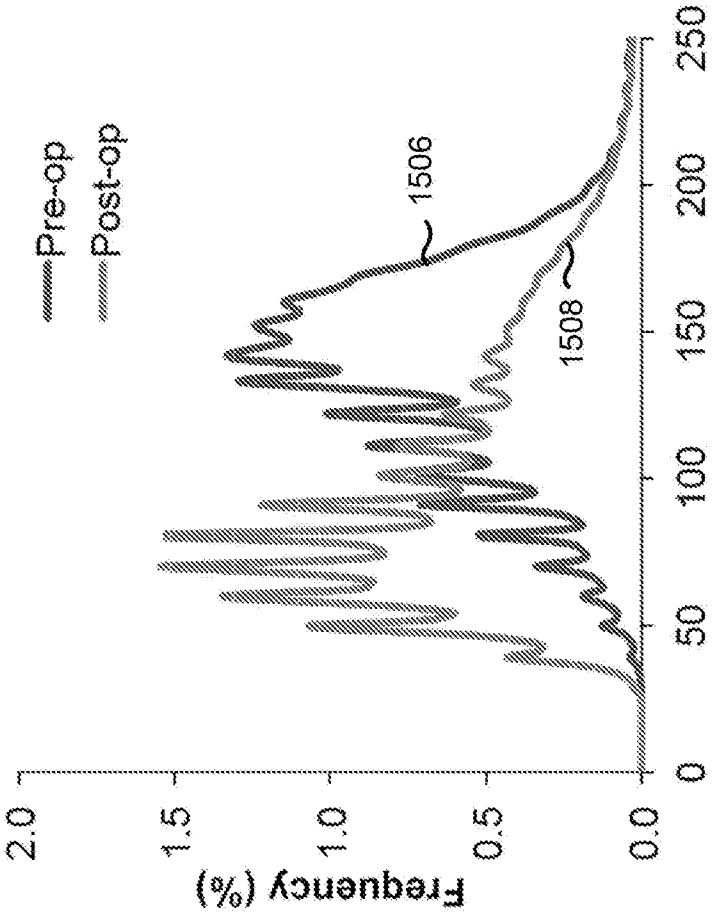


FIG. 15B

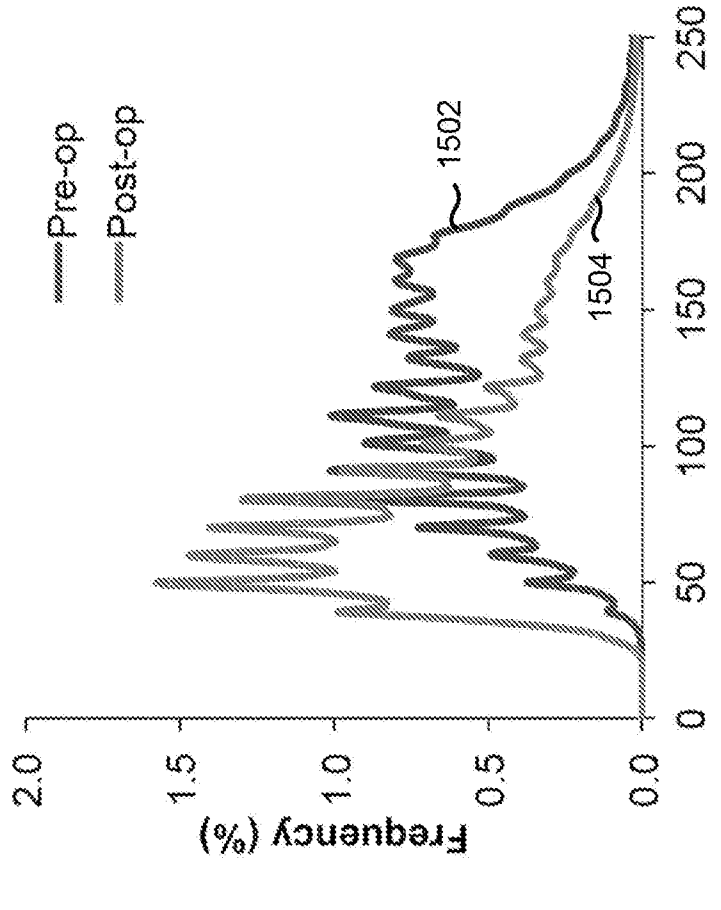


FIG. 15A

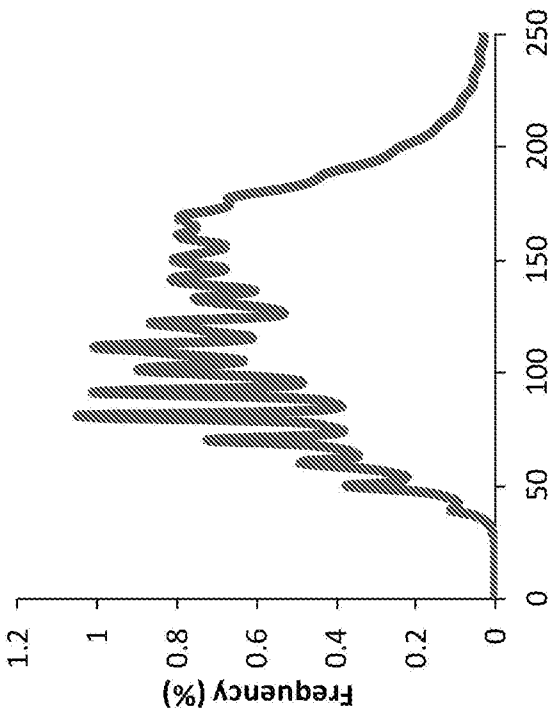


FIG. 16A

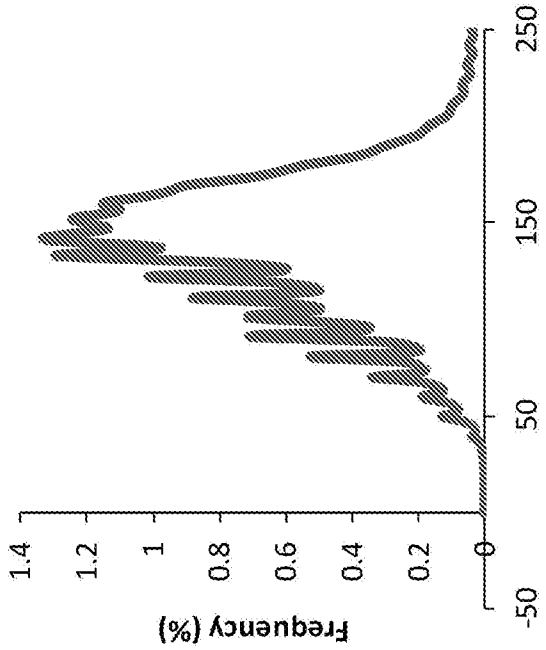


FIG. 16B

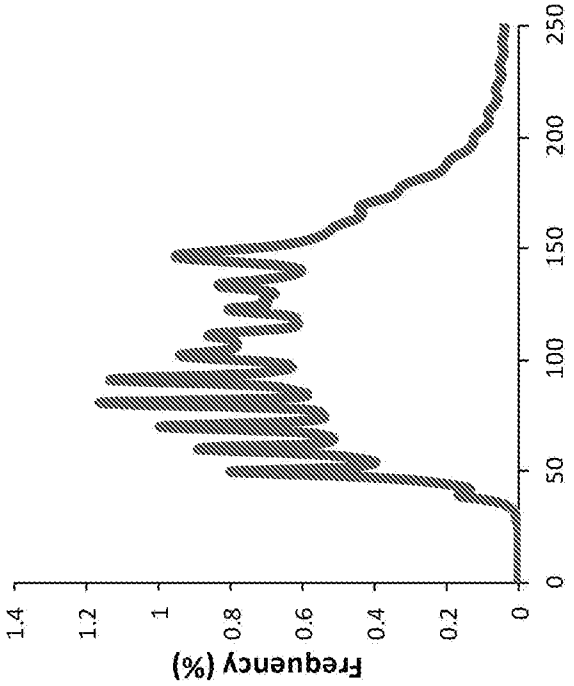


FIG. 16C

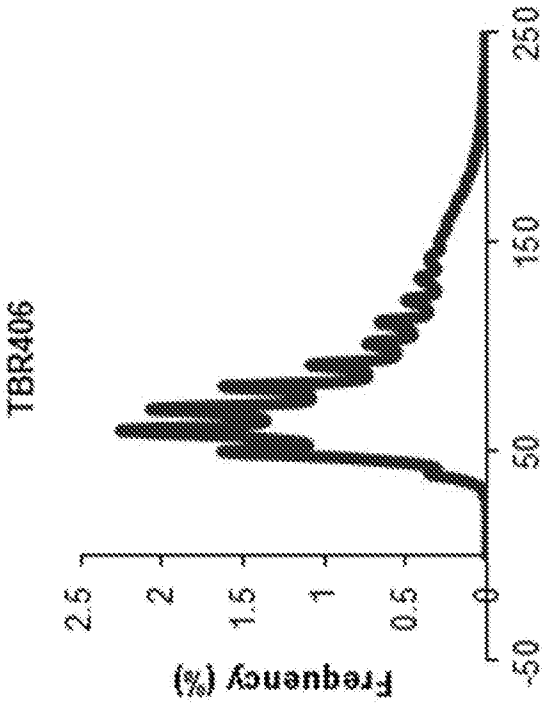


FIG. 17B

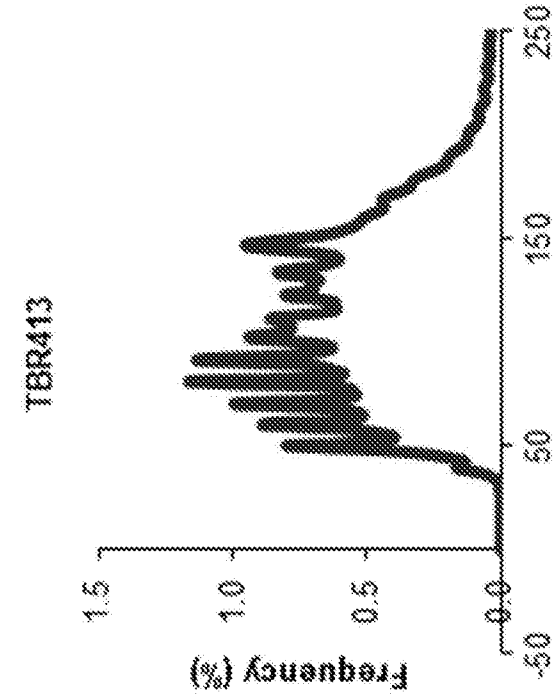


FIG. 17A

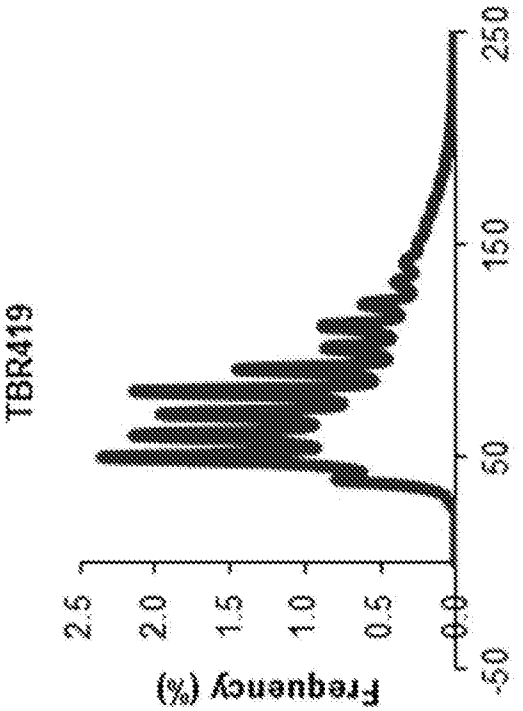


FIG. 17C

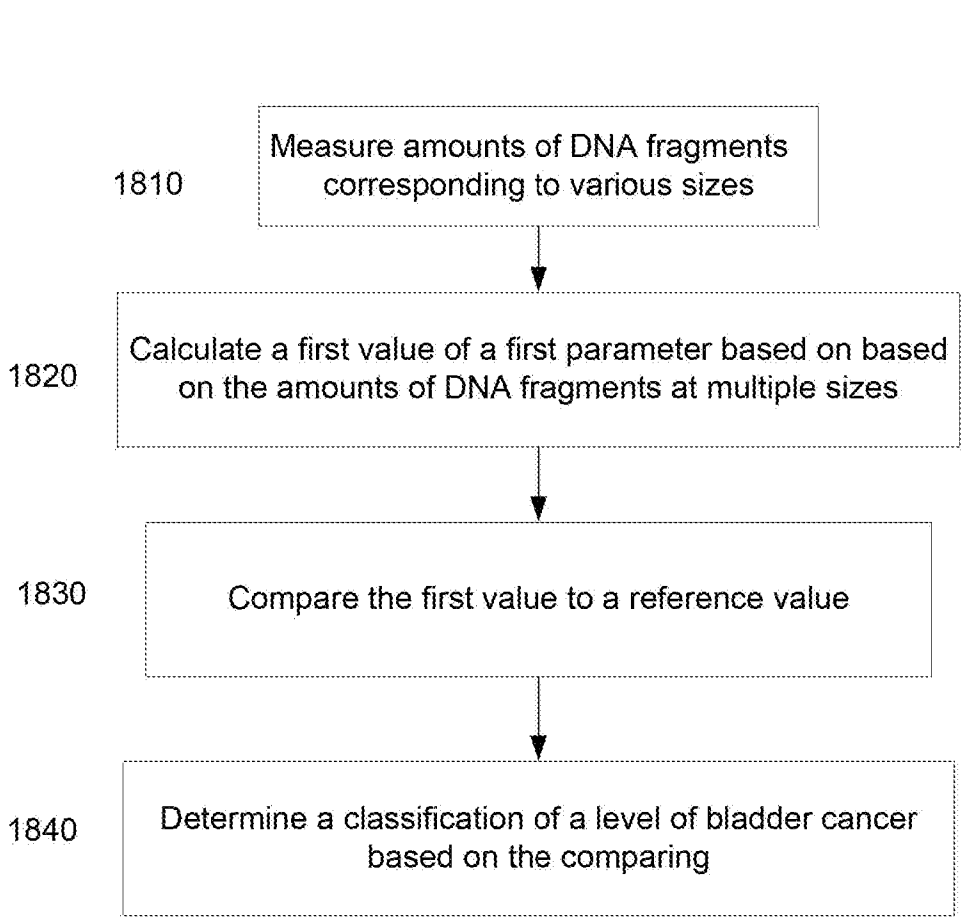

1800
1810
Measure amounts of DNA fragments corresponding to various sizes
1820
Calculate a first value of a first parameter based on based on the amounts of DNA fragments at multiple sizes
1830
Compare the first value to a reference value
1840
Determine a classification of a level of bladder cancer based on the comparing

FIG. 18

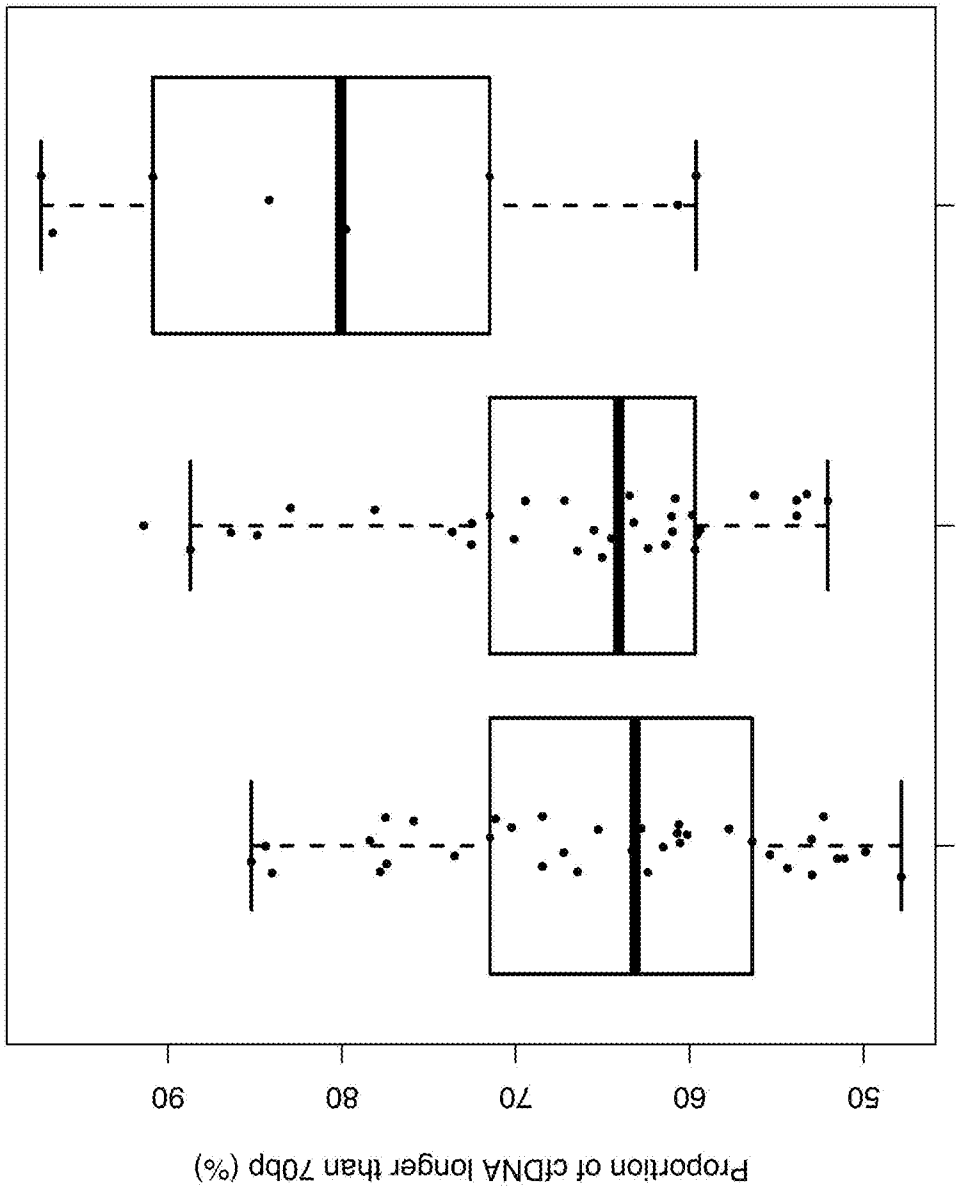

Proportion of cfDNA longer than 70bp (%)
50
60
70
80
90
Controls
Ta–T1
T2–4

FIG. 19A

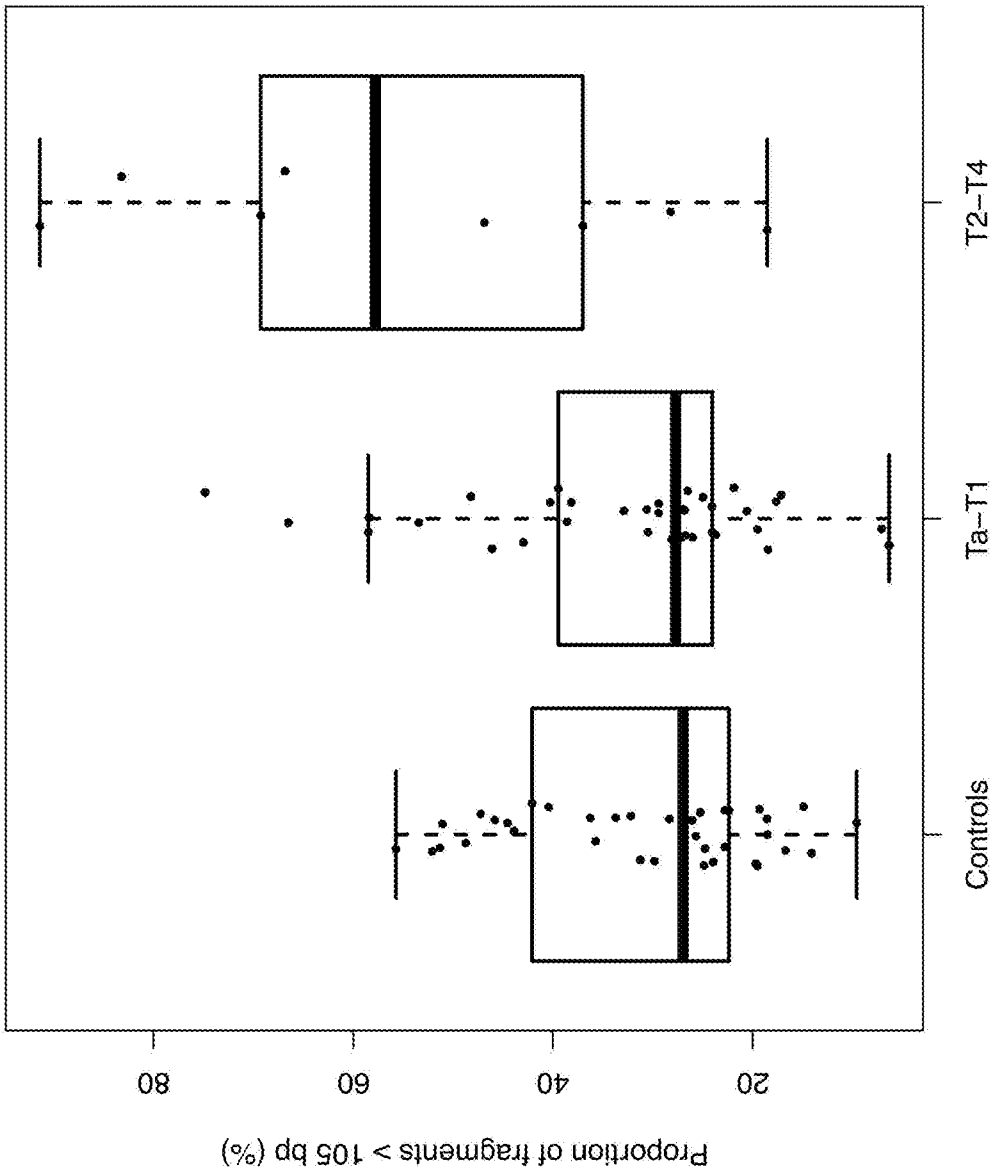

Proportion of fragments > 105 bp (%)
20
40
60
80
Controls
Ta–T1
T2–T4

FIG. 19B

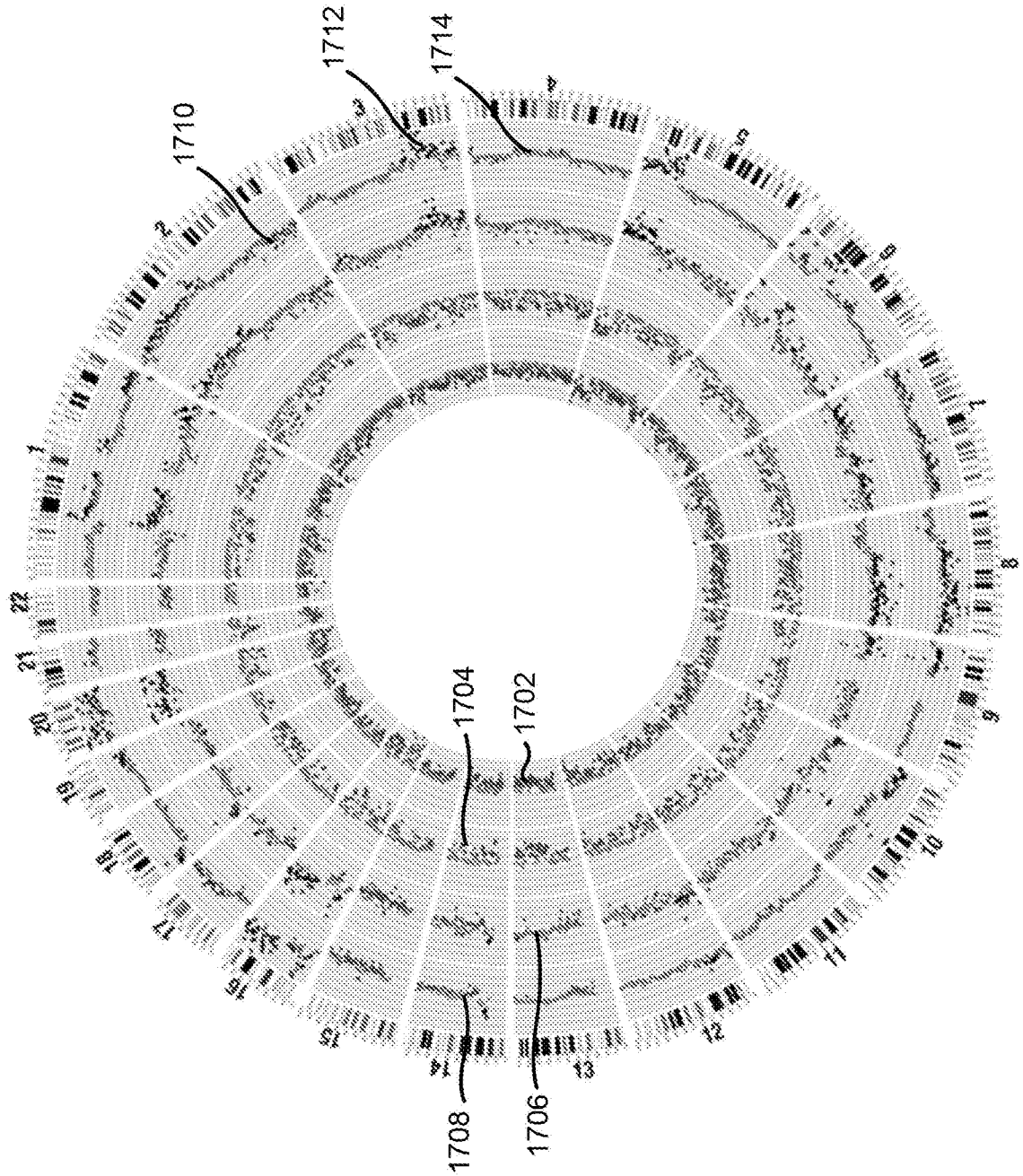


FIG. 20

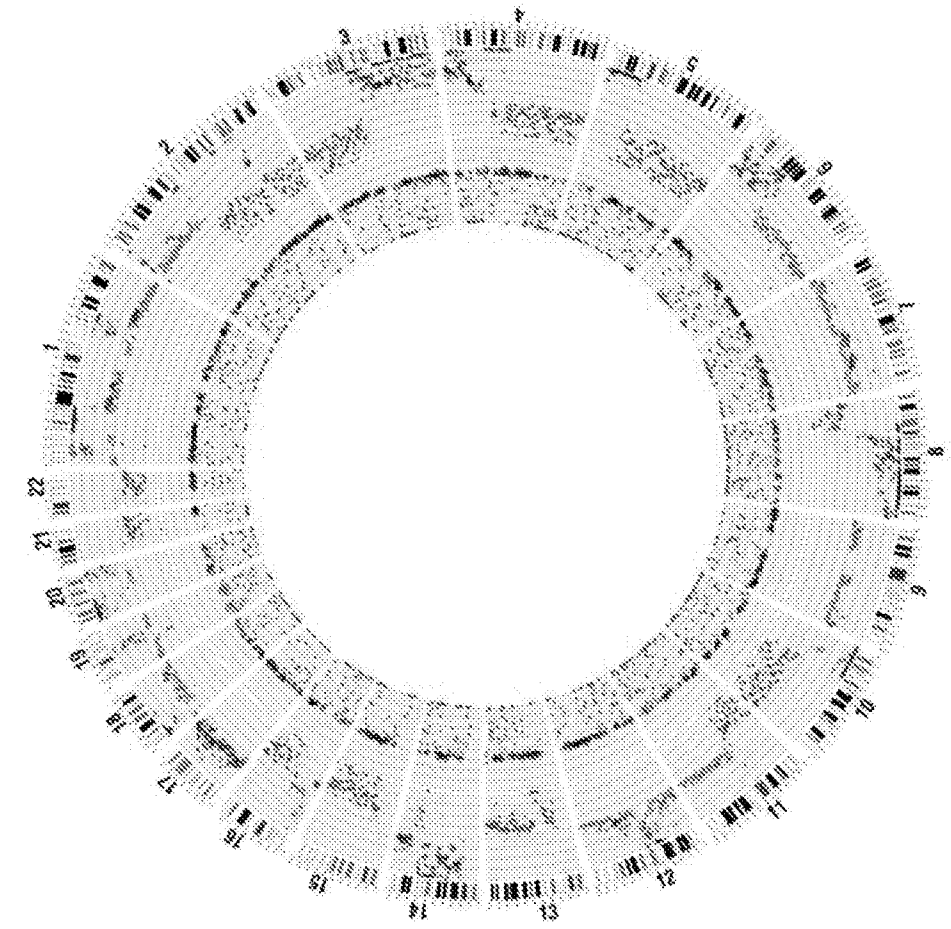


FIG. 21B

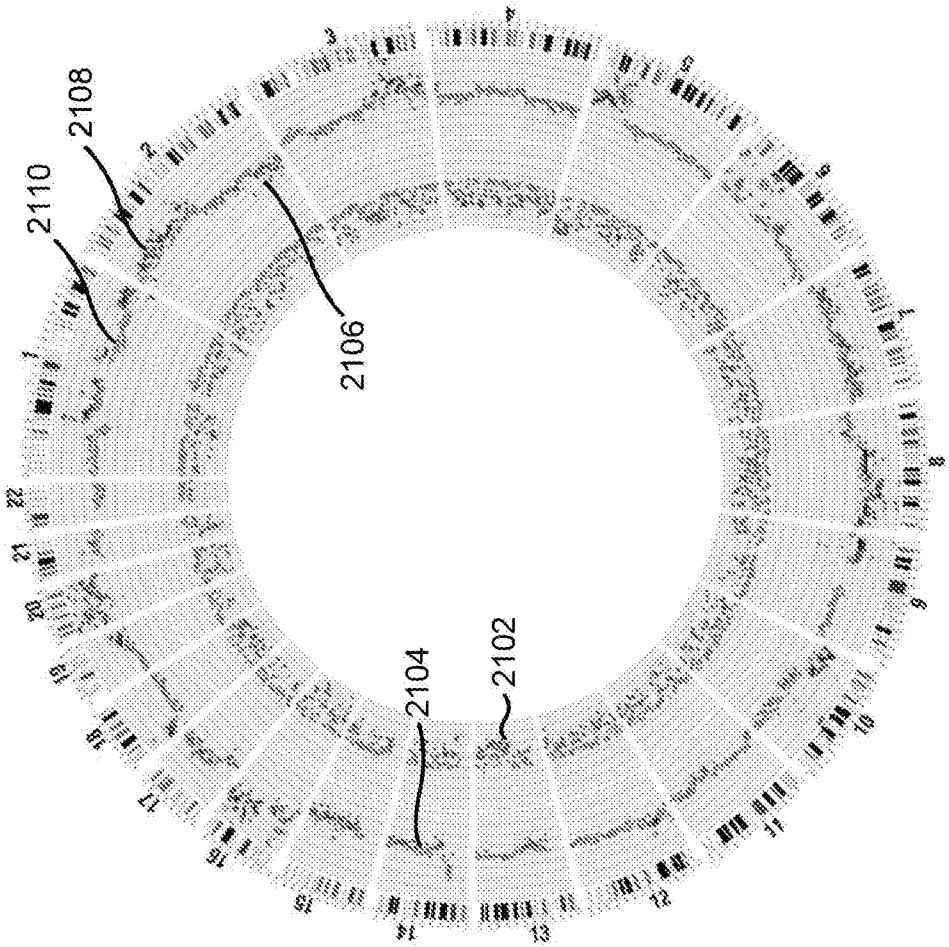


FIG. 21A

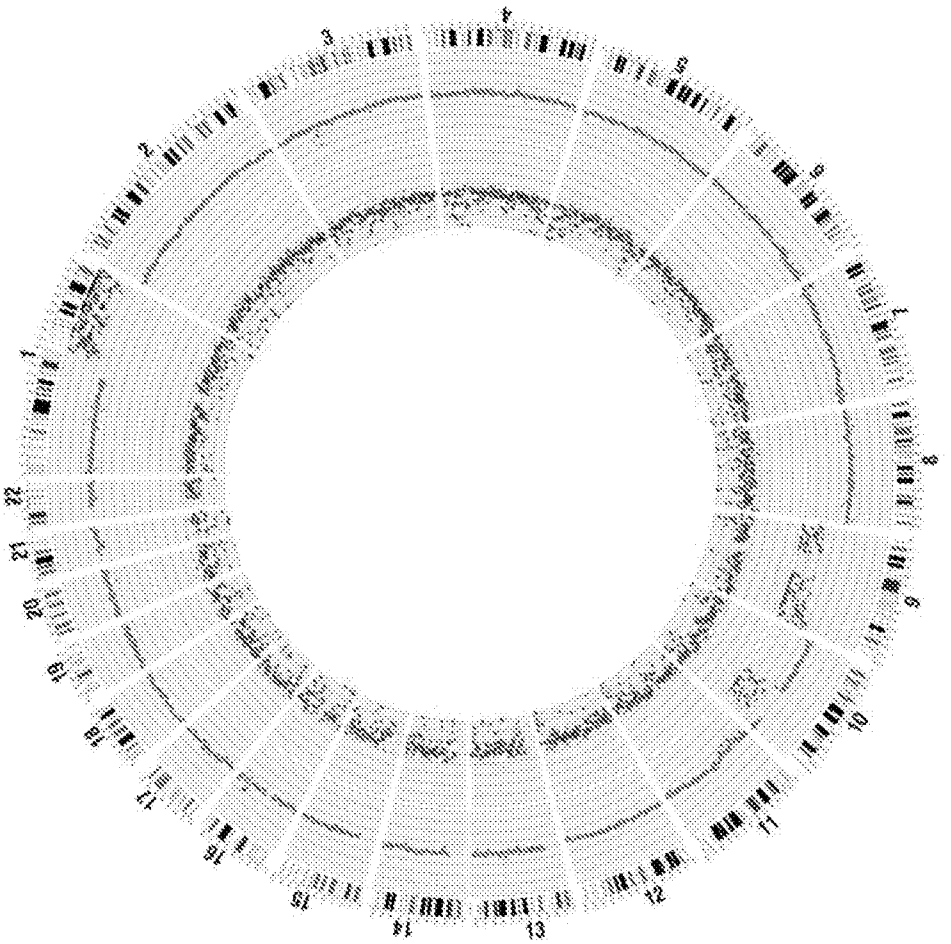


FIG. 21D

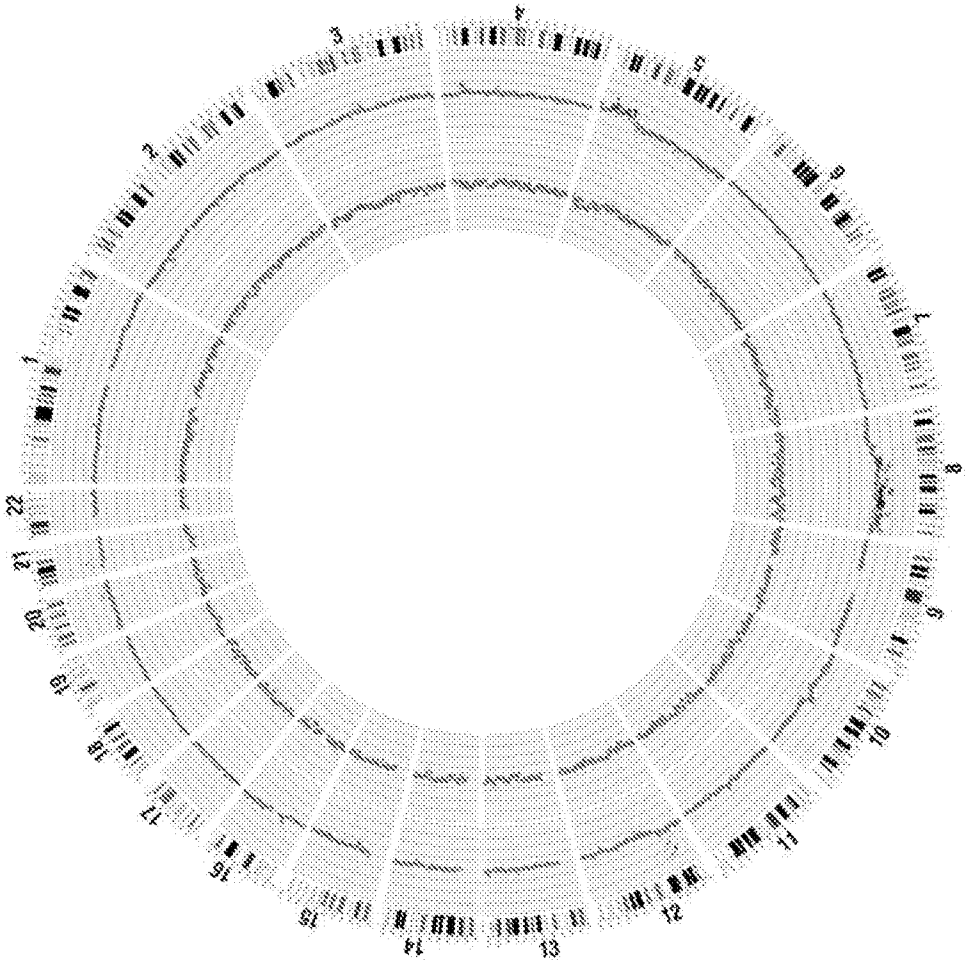


FIG. 21C

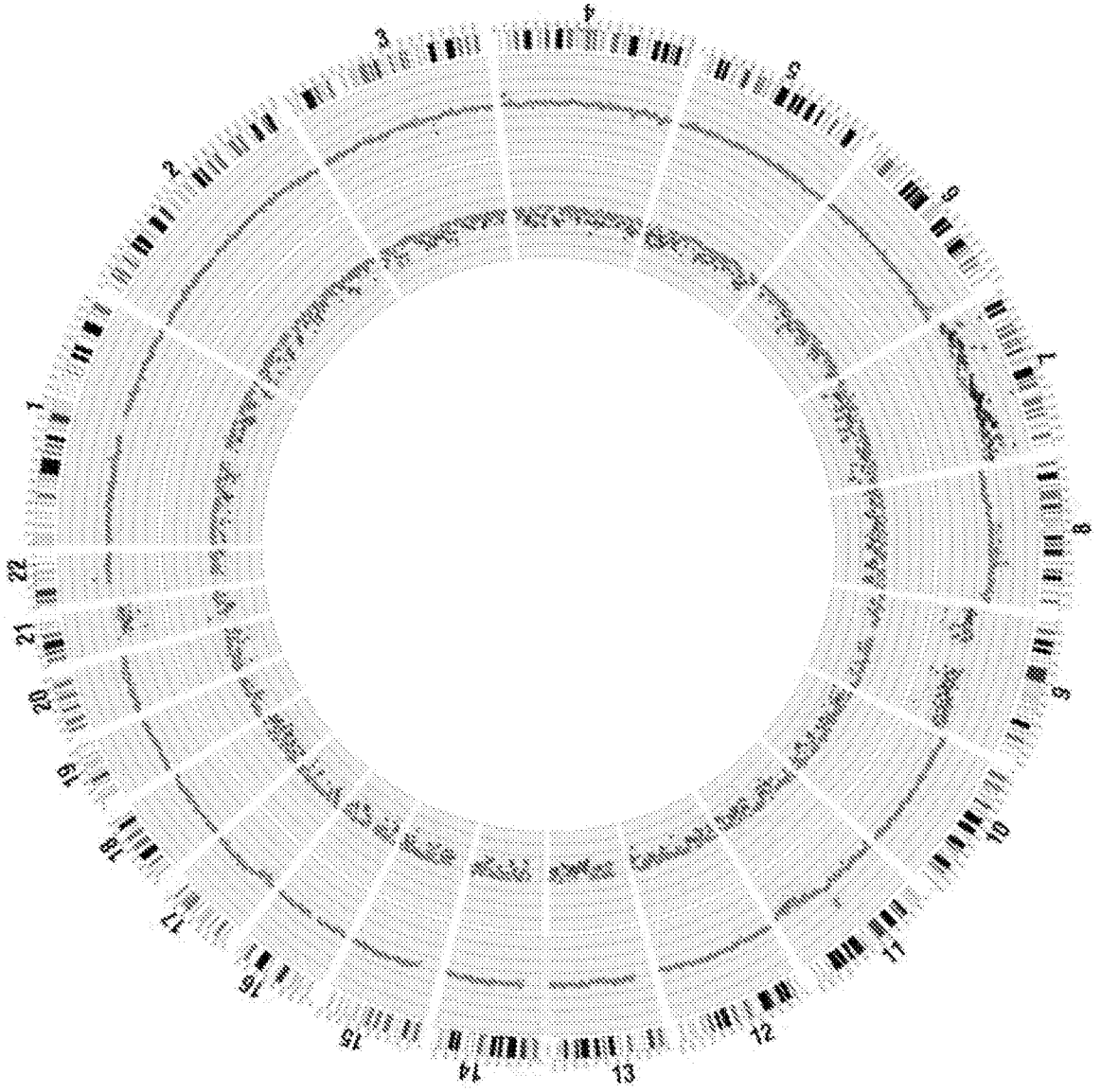


FIG. 21E

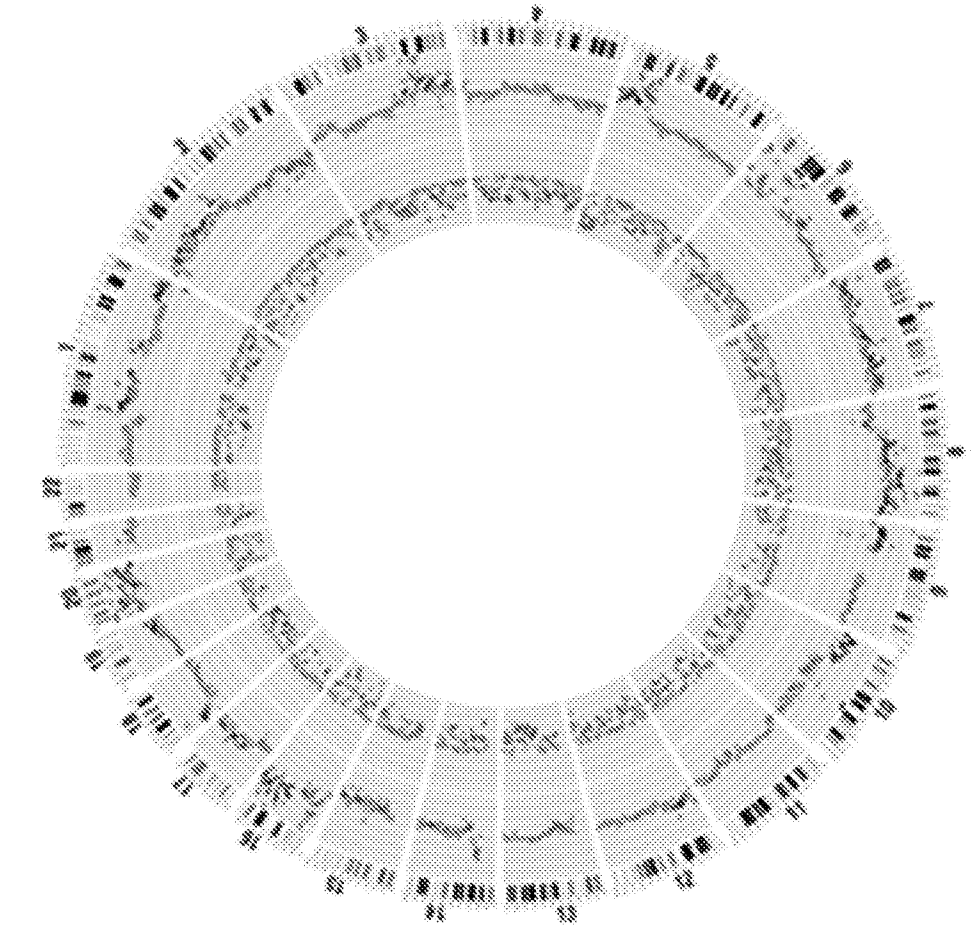


FIG. 22B

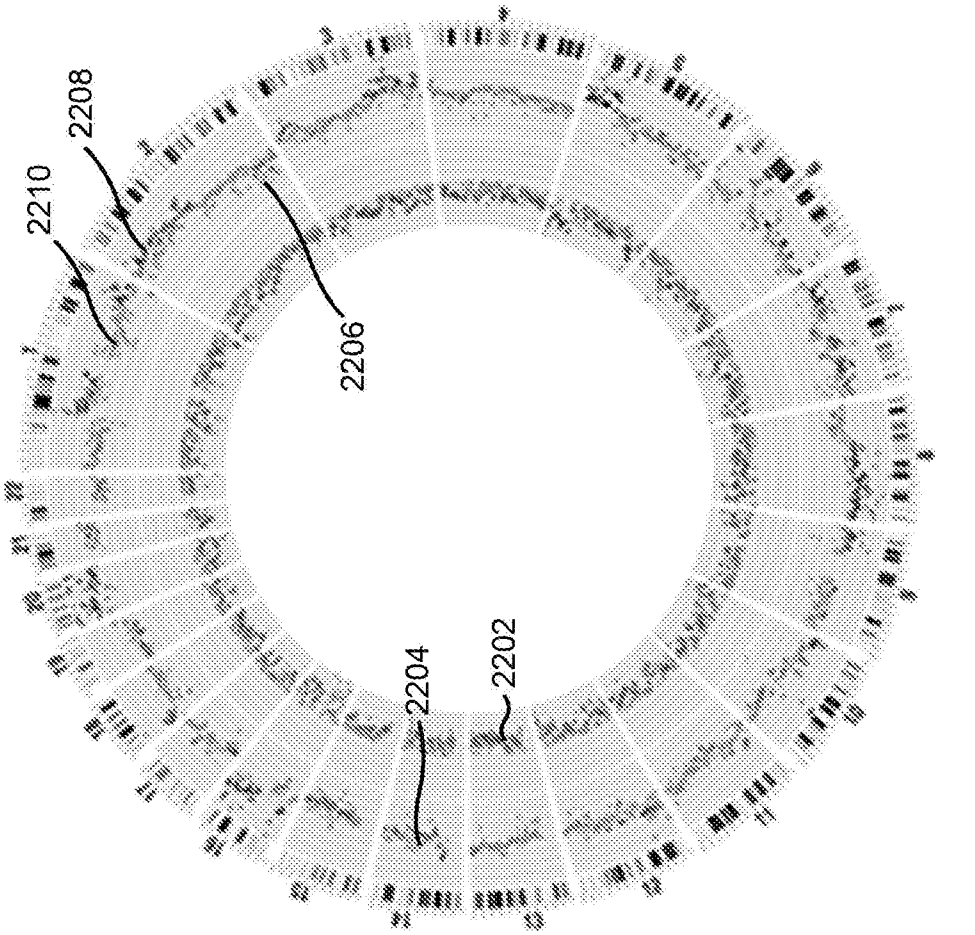


FIG. 22A

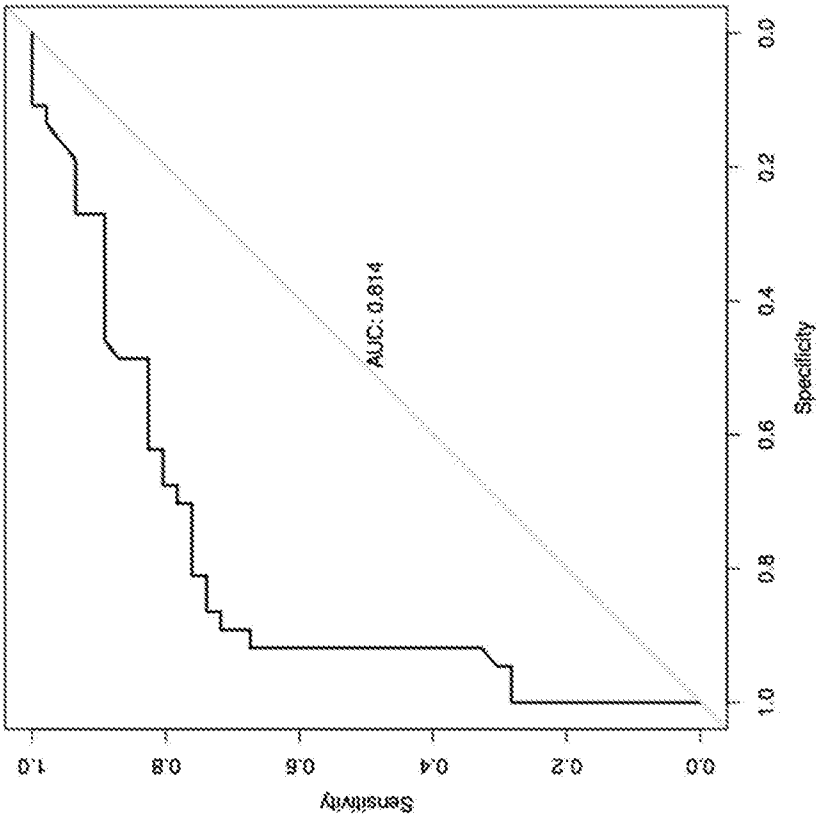


FIG. 23B

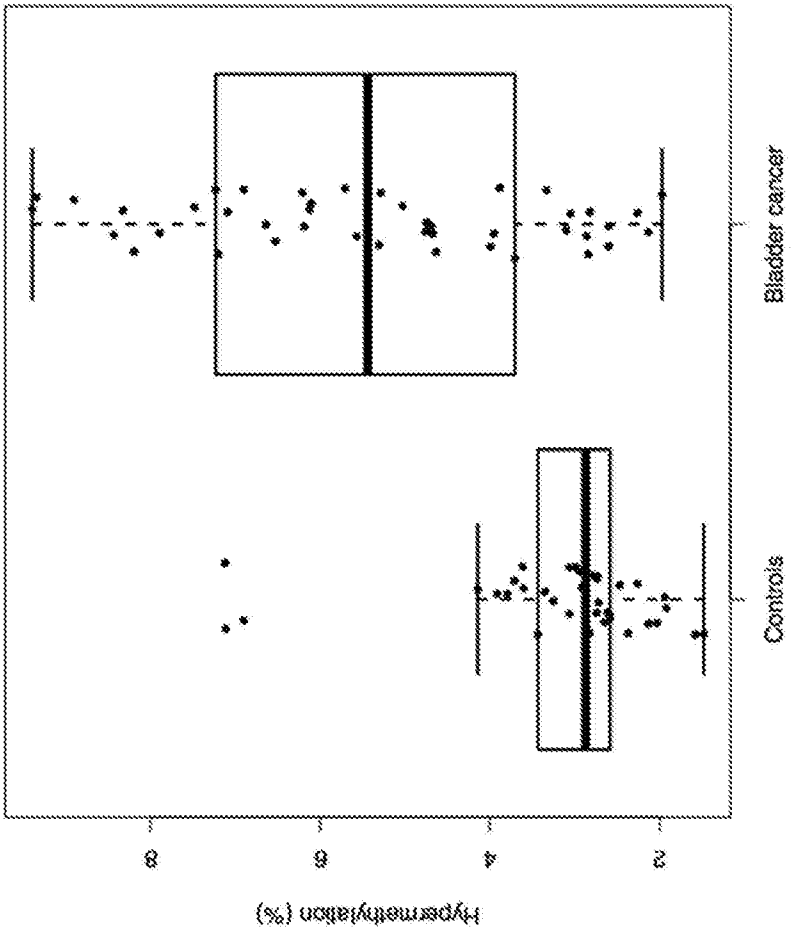


FIG. 23A

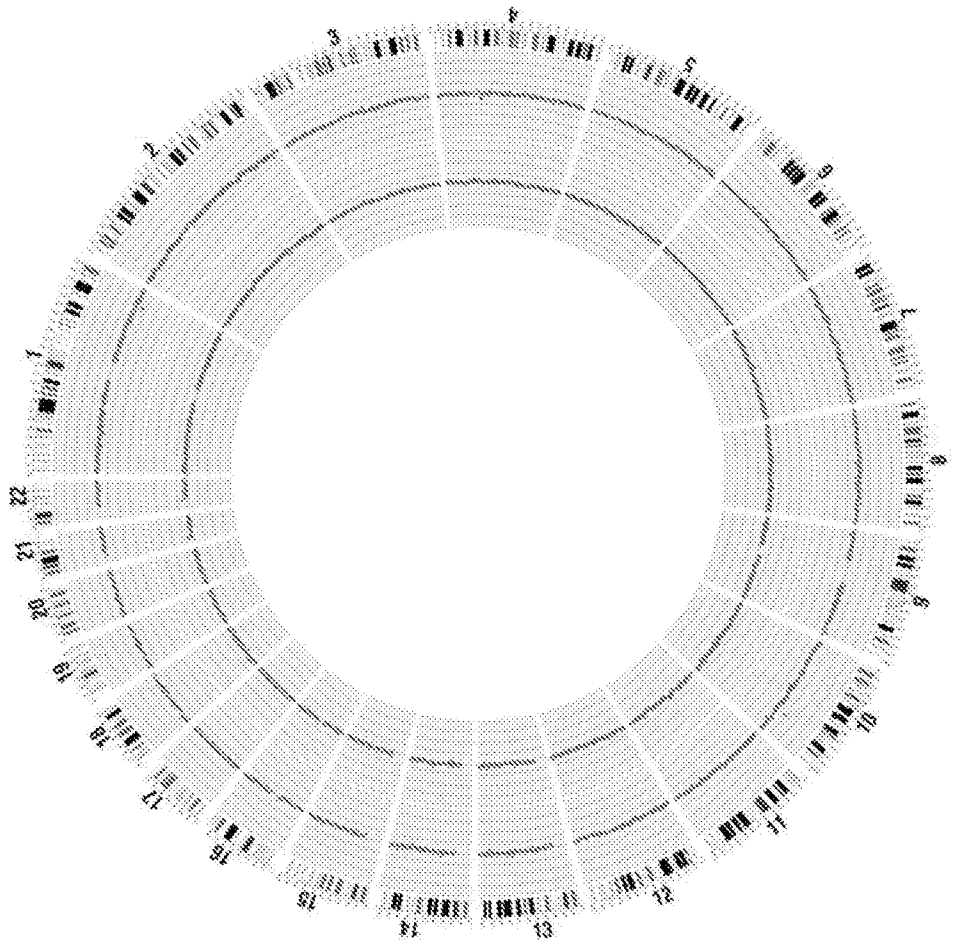


FIG. 24B

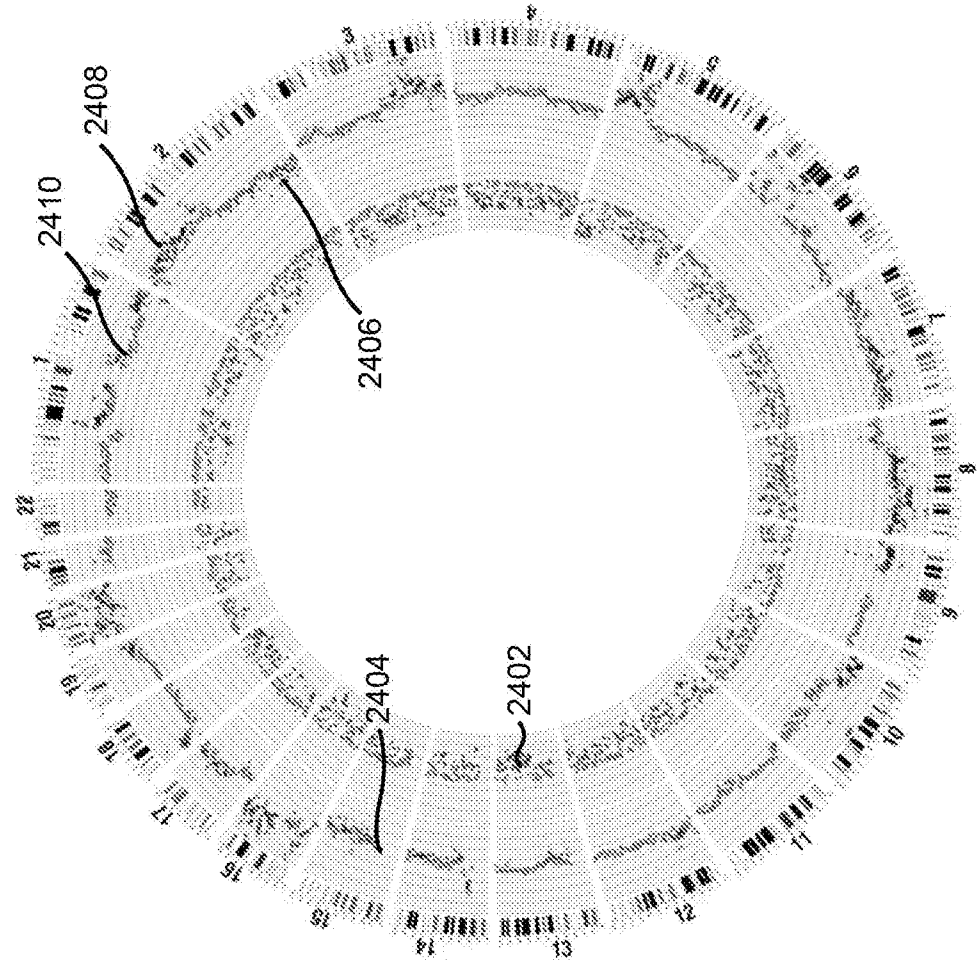


FIG. 24A

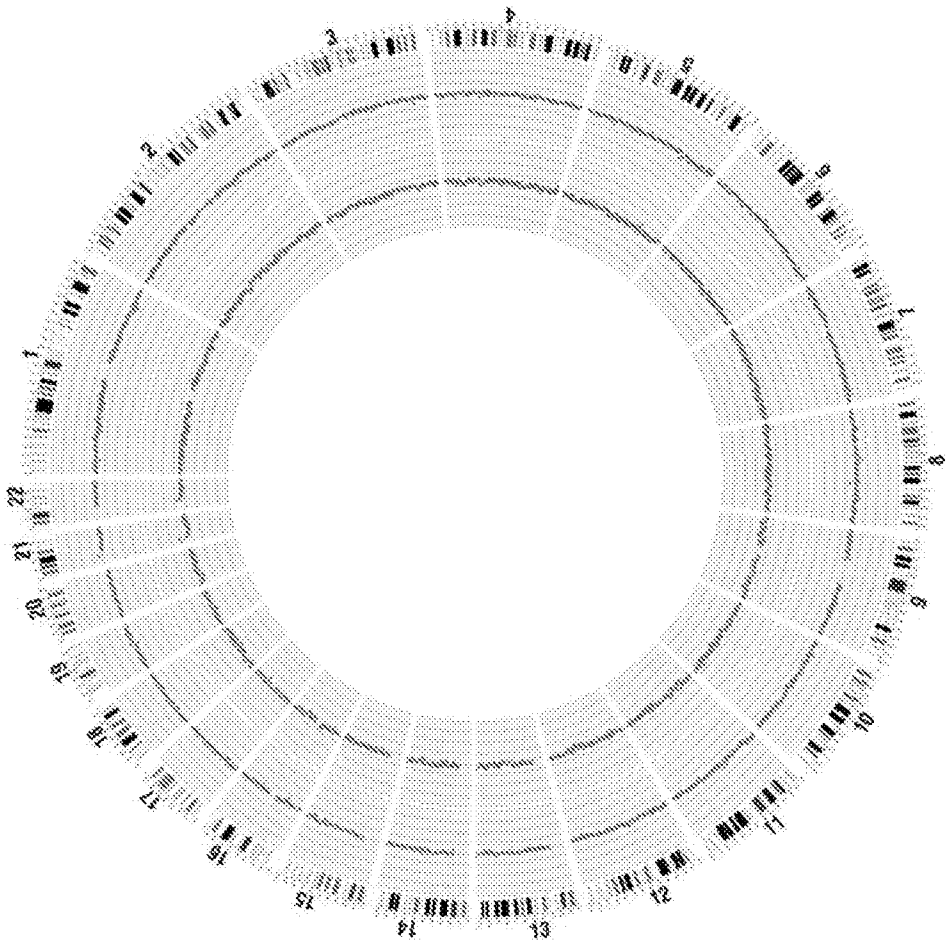


FIG. 24D

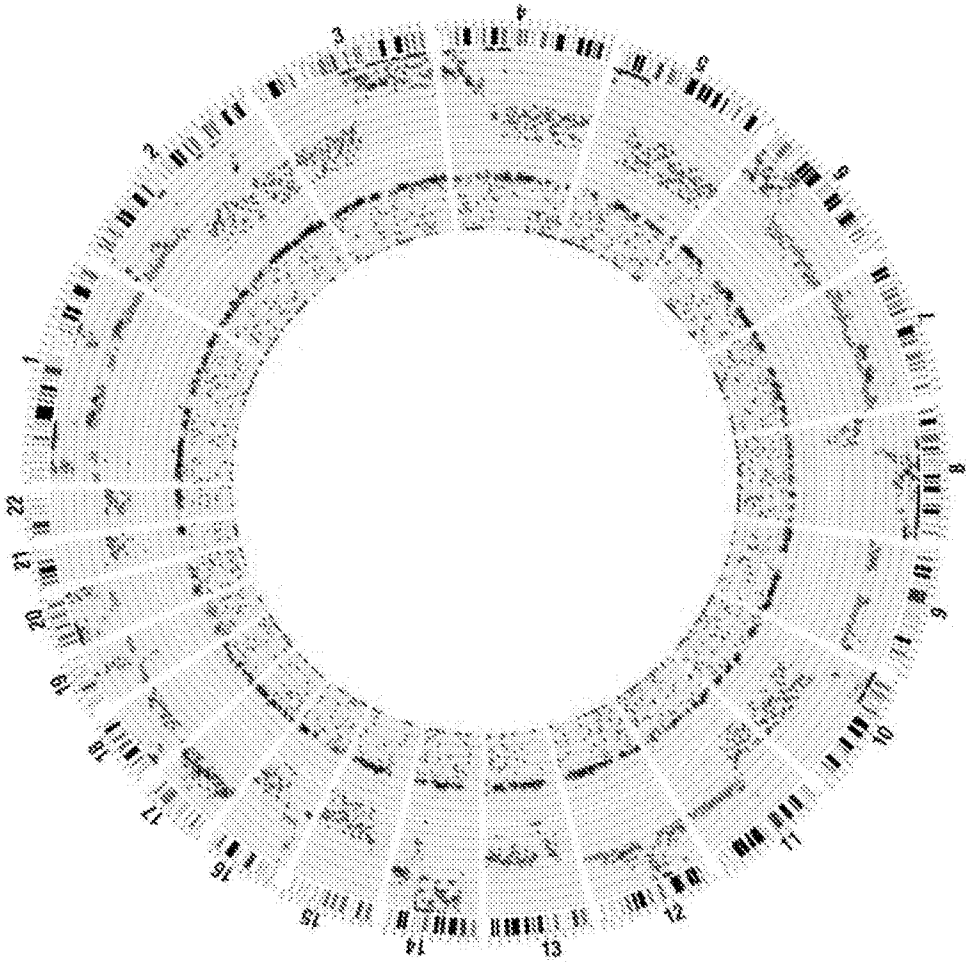


FIG. 24C

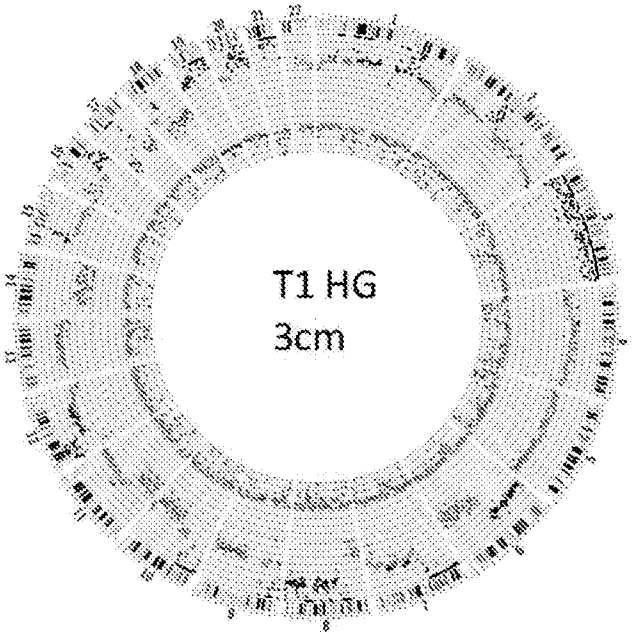


FIG. 25A

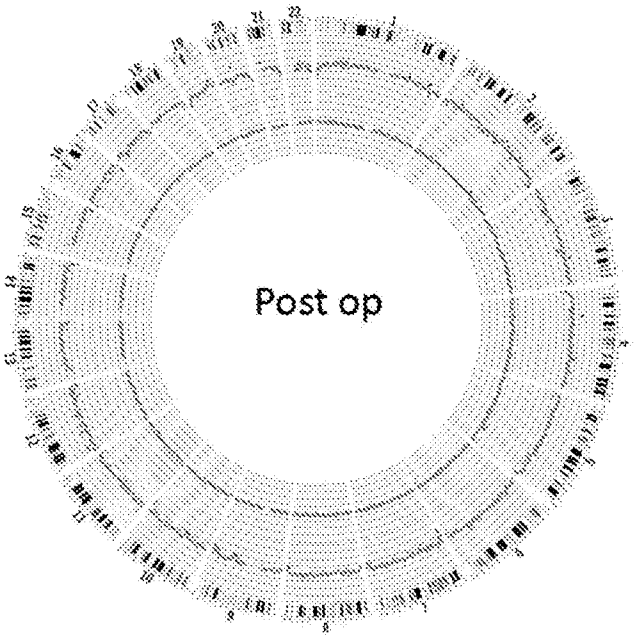


FIG. 25B

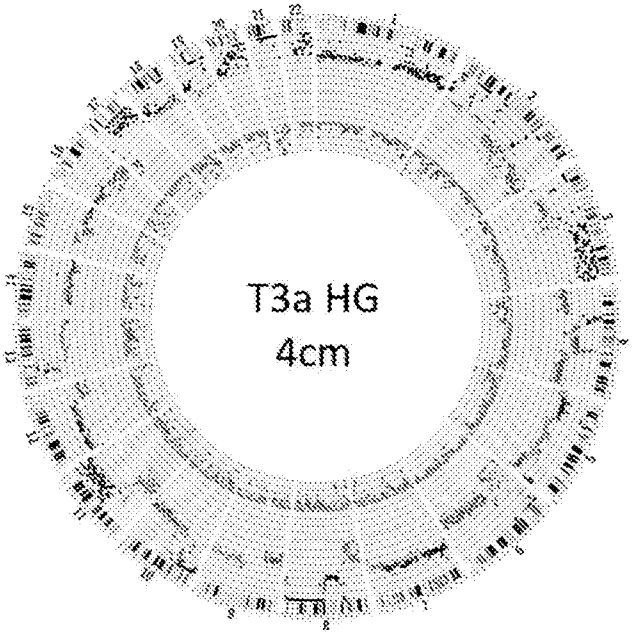


FIG. 25C

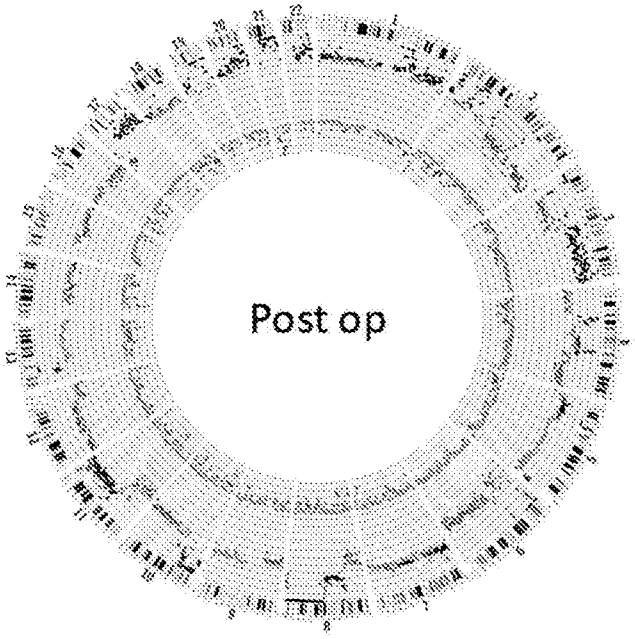


FIG. 25D

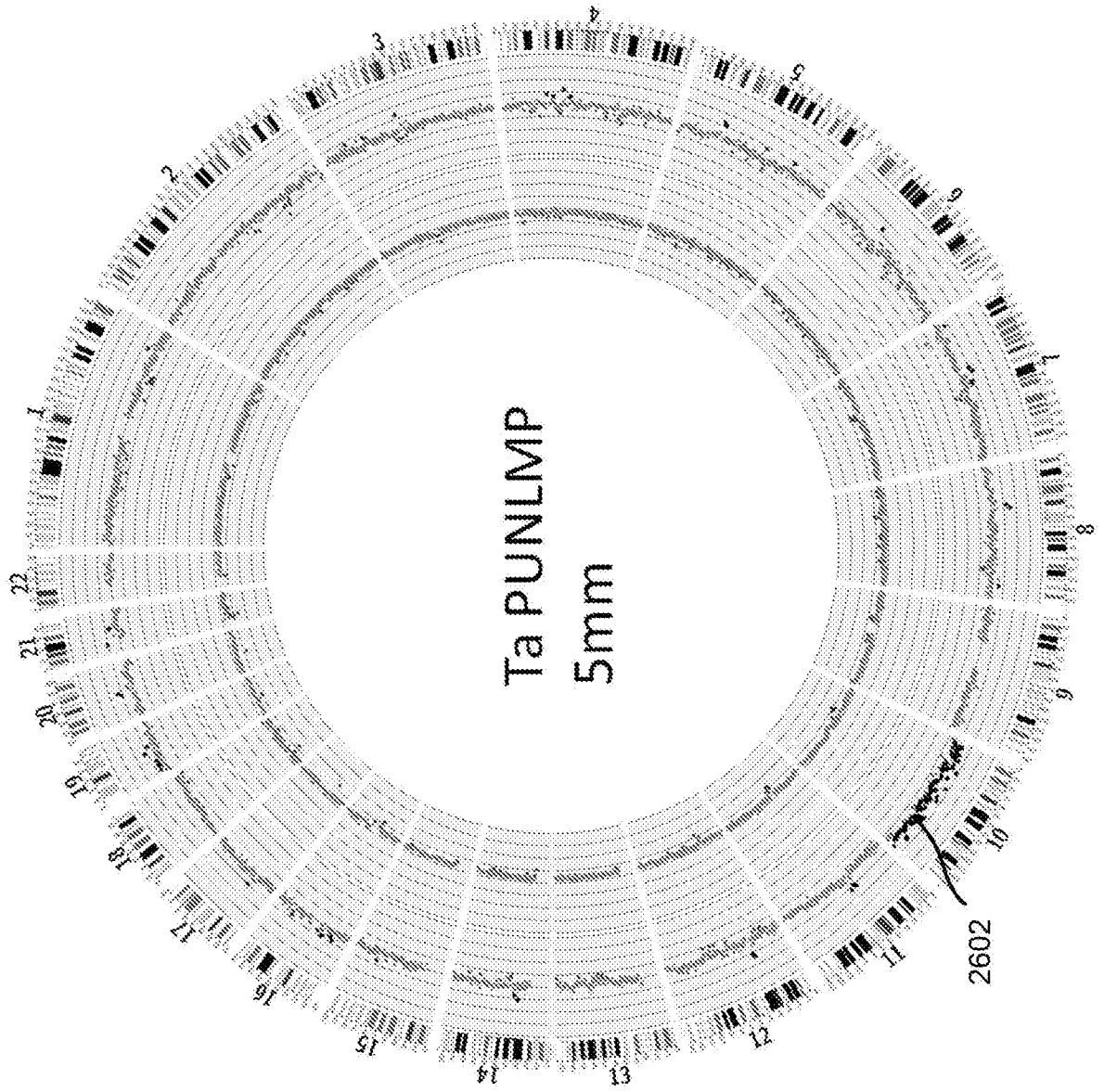

Ta PUNLMP
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2602

FIG. 26

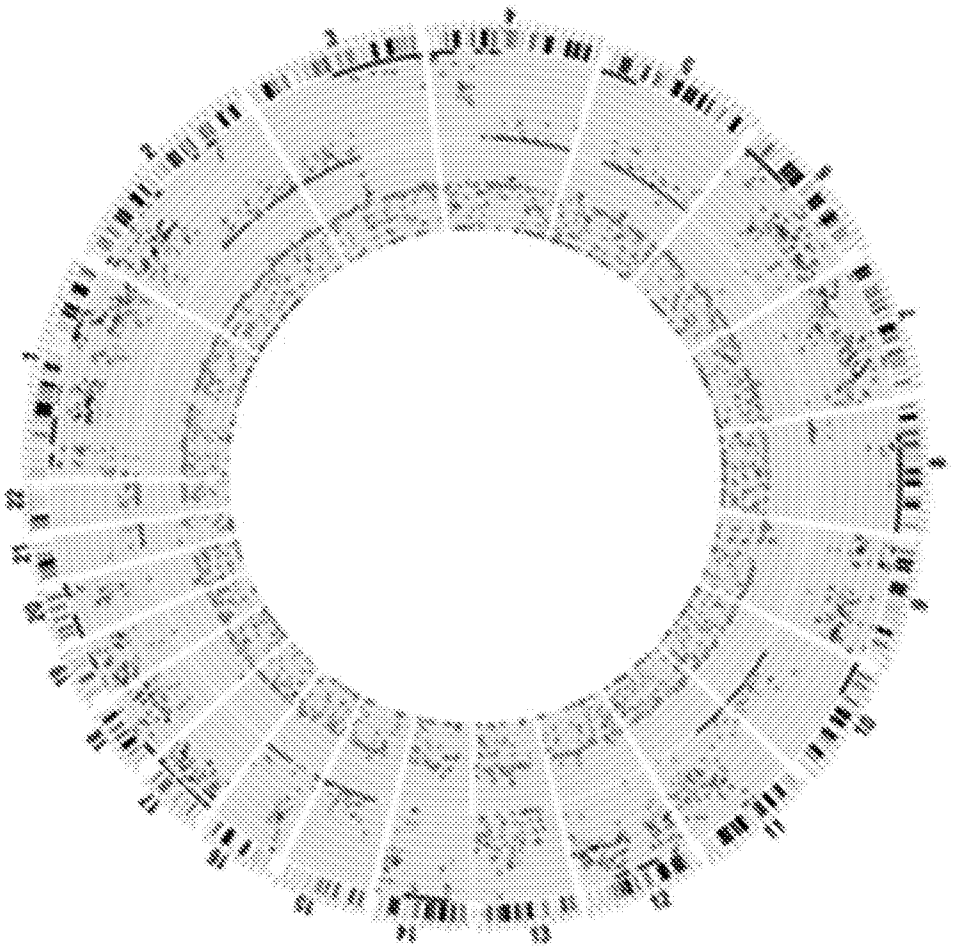


FIG. 27B

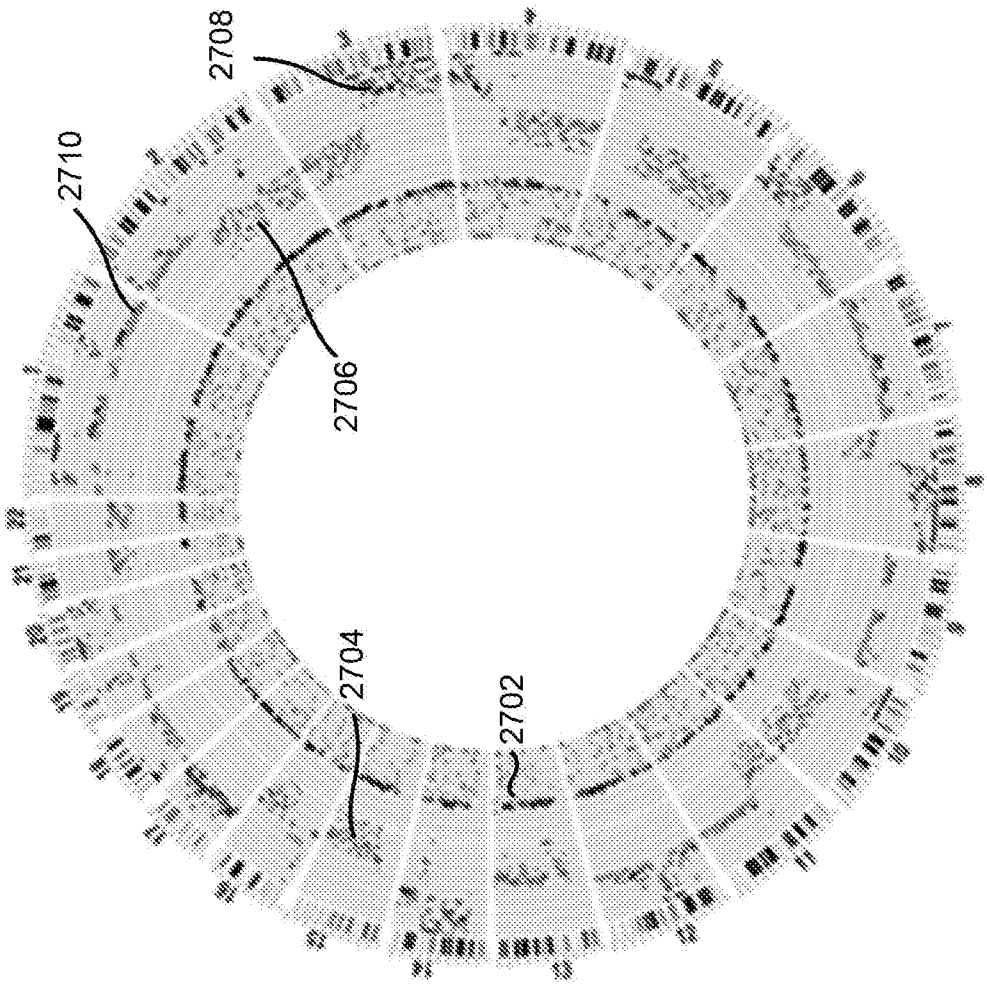


FIG. 27A

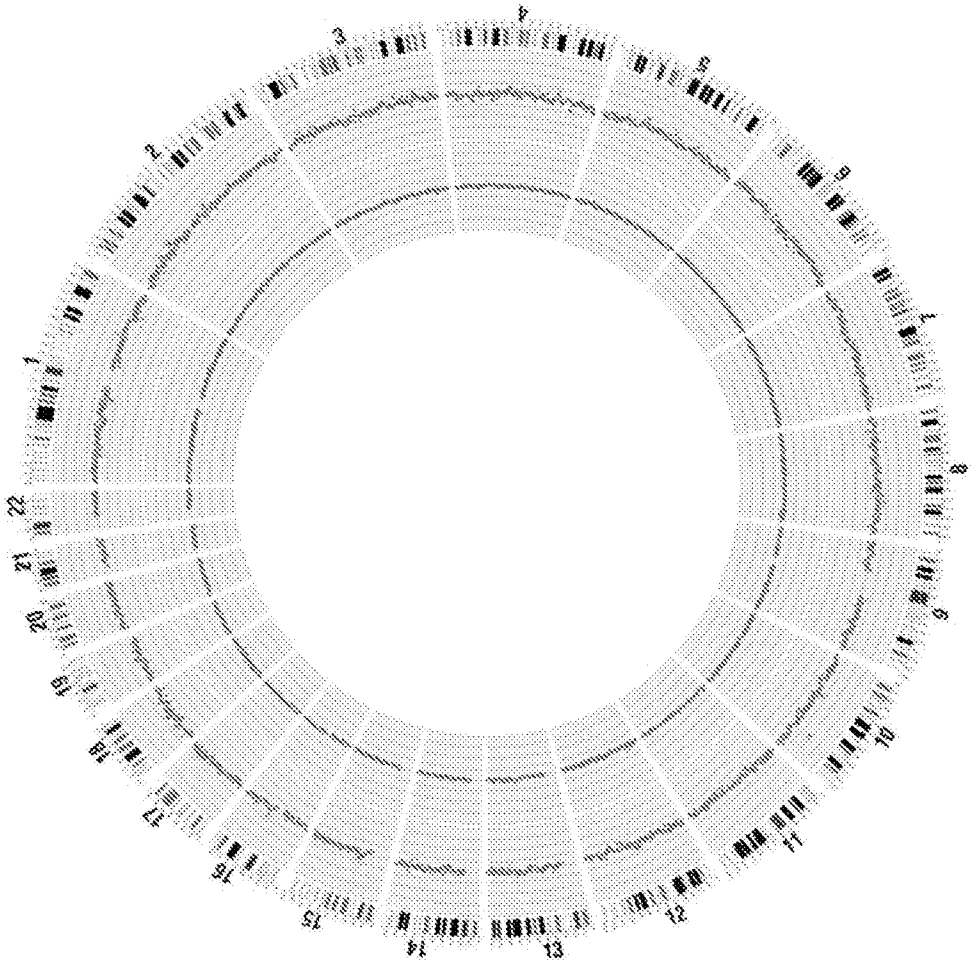


FIG. 28B

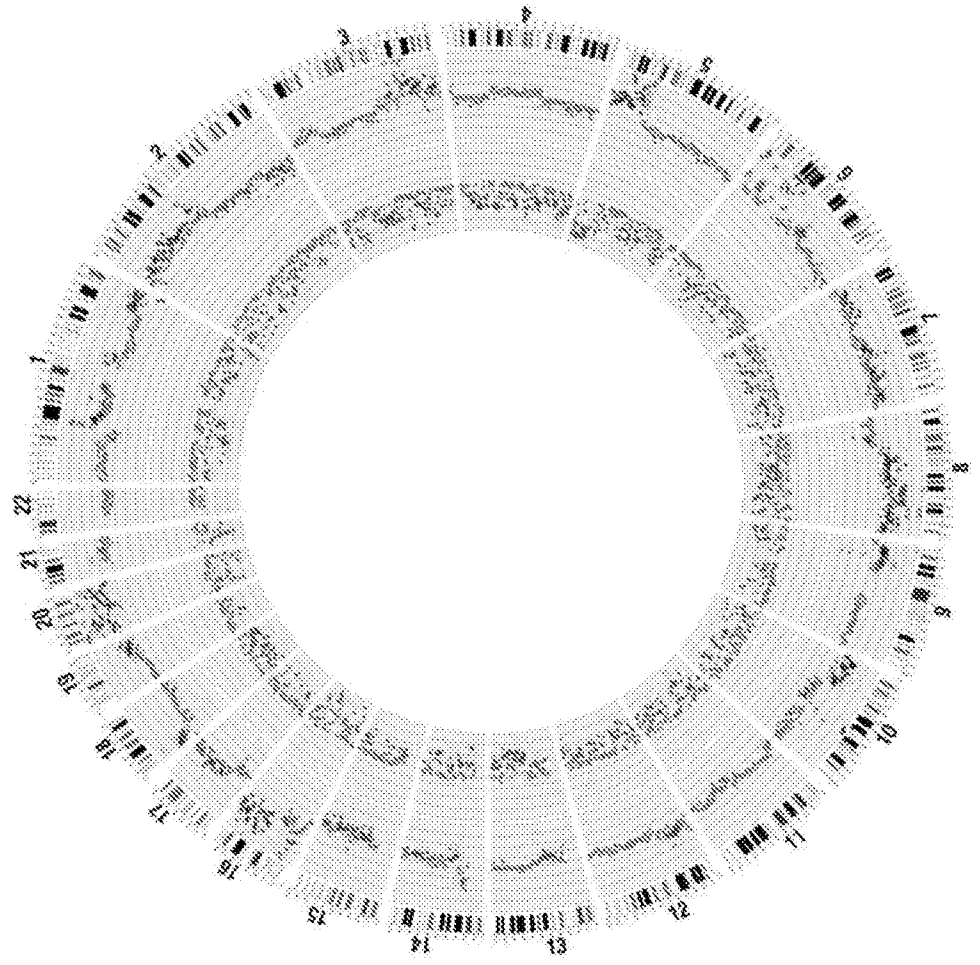


FIG. 28A

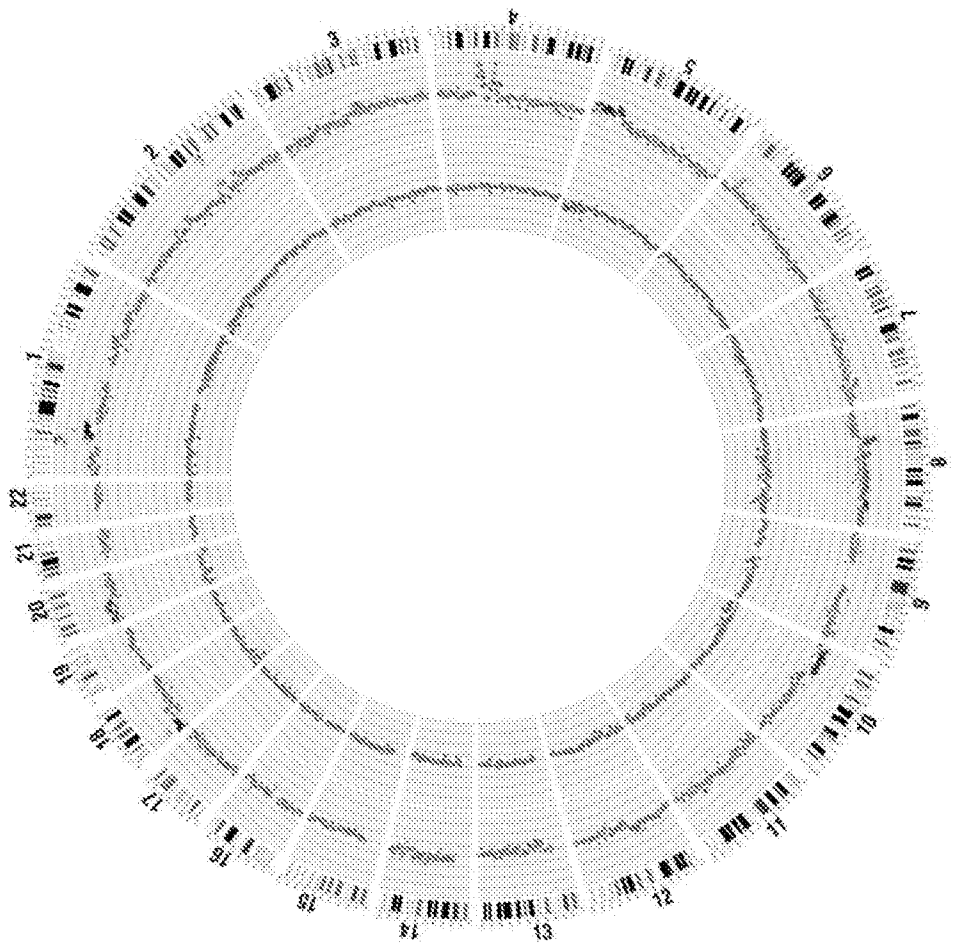


FIG. 28D

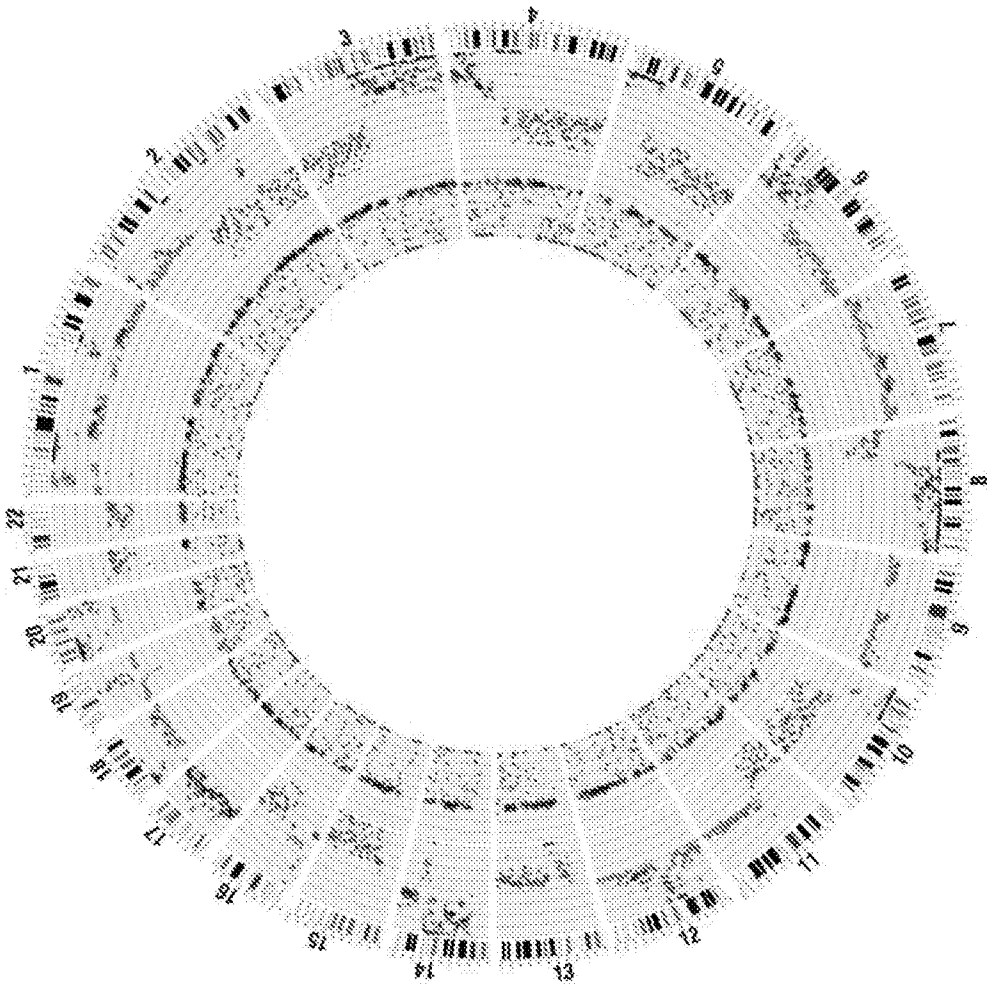


FIG. 28C

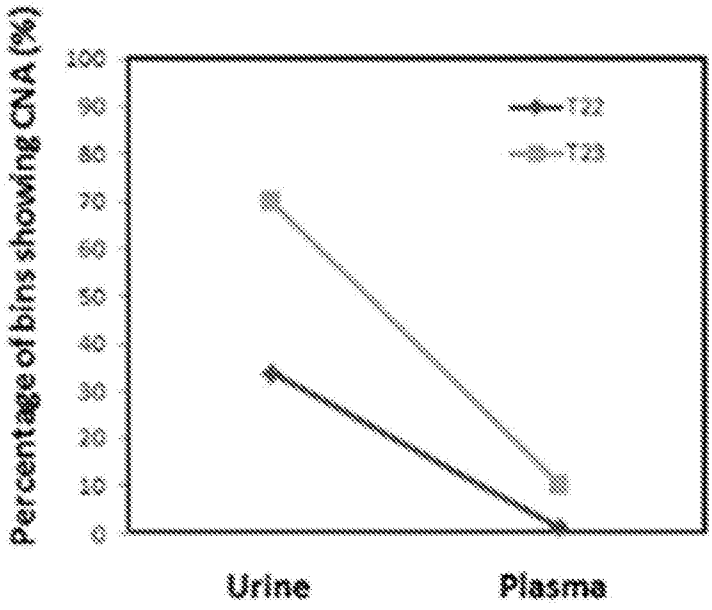


FIG. 29A

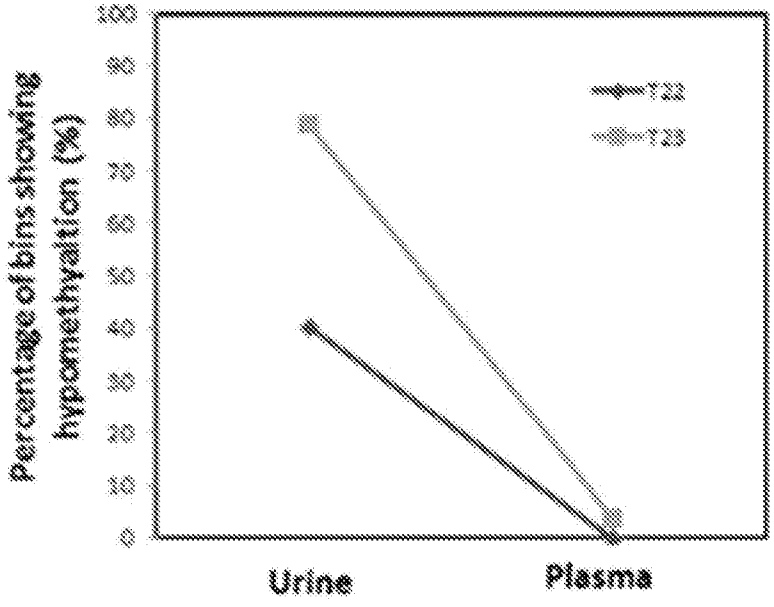


FIG. 29B

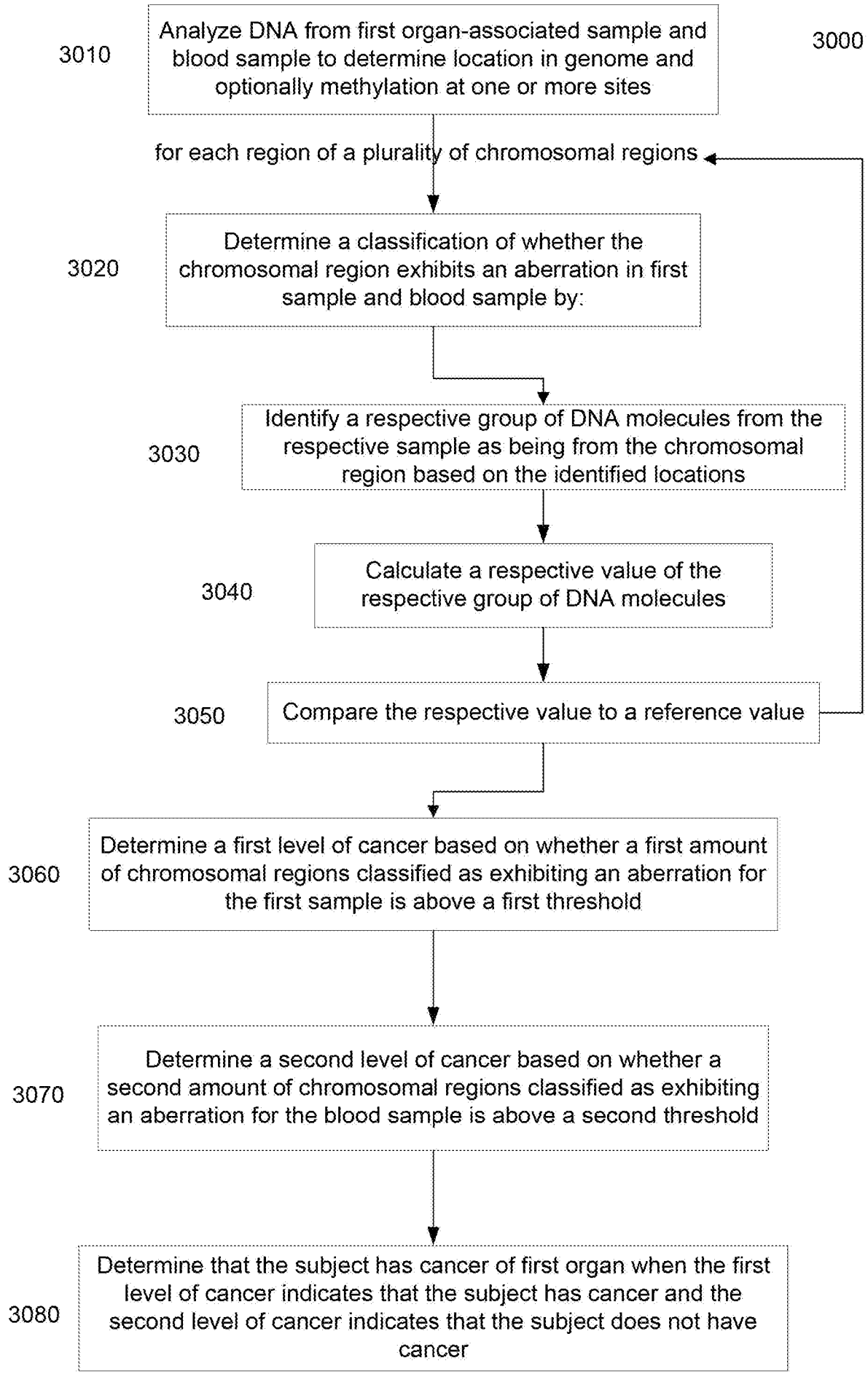

3000
3010
Analyze DNA from first organ-associated sample and blood sample to determine location in genome and optionally methylation at one or more sites
for each region of a plurality of chromosomal regions
3020
Determine a classification of whether the chromosomal region exhibits an aberration in first sample and blood sample by:
3030
Identify a respective group of DNA molecules from the respective sample as being from the chromosomal region based on the identified locations
3040
Calculate a respective value of the respective group of DNA molecules
3050
Compare the respective value to a reference value
3060
Determine a first level of cancer based on whether a first amount of chromosomal regions classified as exhibiting an aberration for the first sample is above a first threshold
3070
Determine a second level of cancer based on whether a second amount of chromosomal regions classified as exhibiting an aberration for the blood sample is above a second threshold
3080
Determine that the subject has cancer of first organ when the first level of cancer indicates that the subject has cancer and the second level of cancer indicates that the subject does not have cancer

FIG. 30

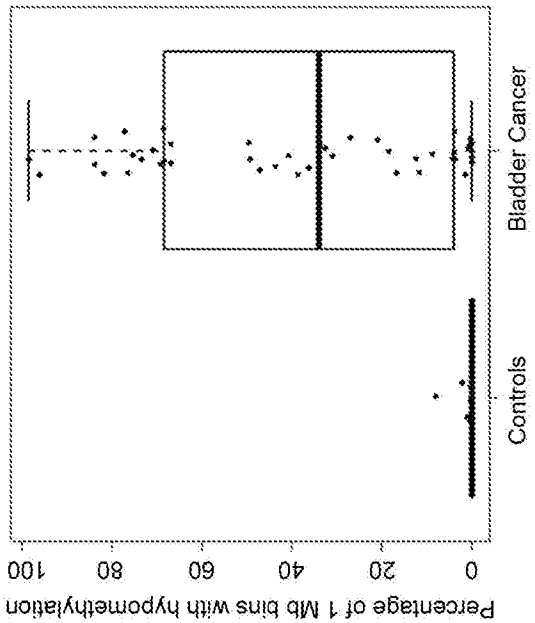


FIG. 31A

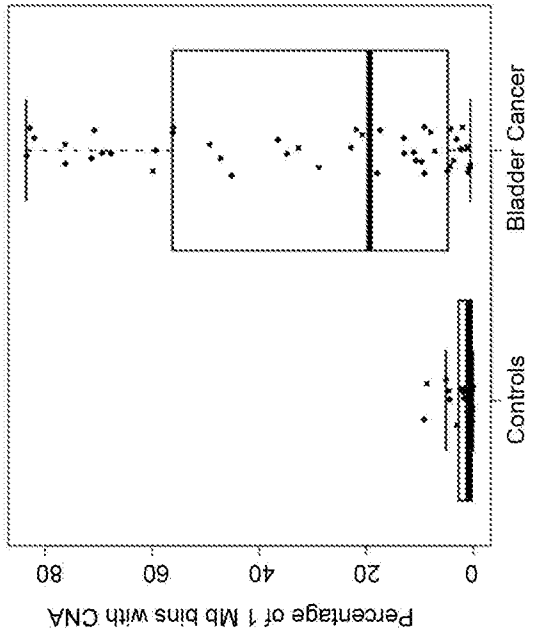


FIG. 31B

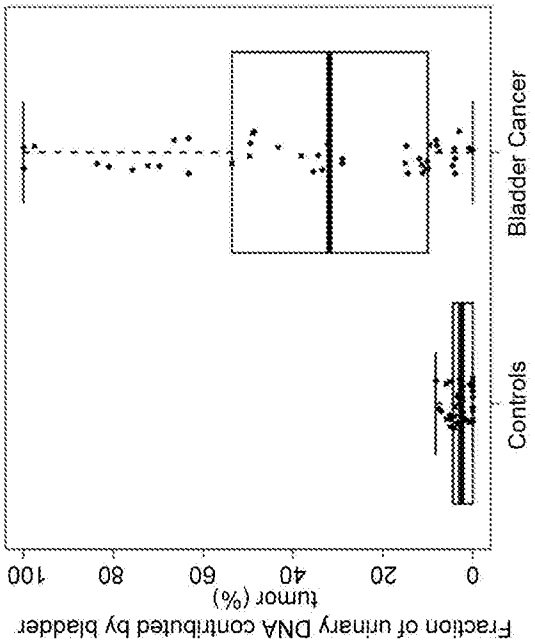


FIG. 31C

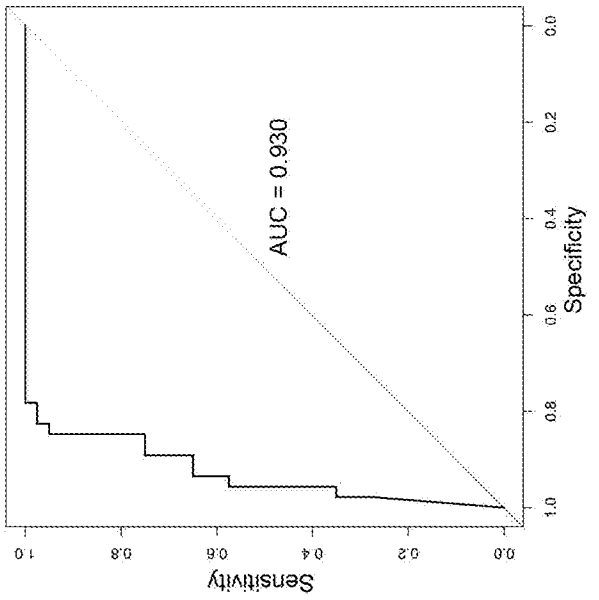


FIG. 31F

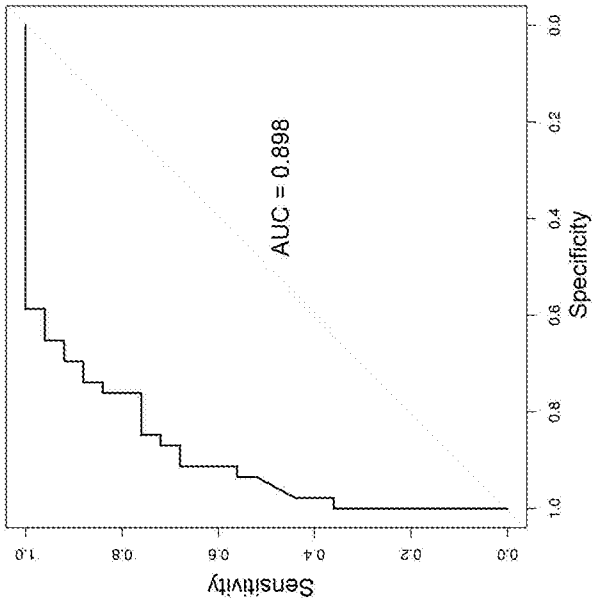


FIG. 31E

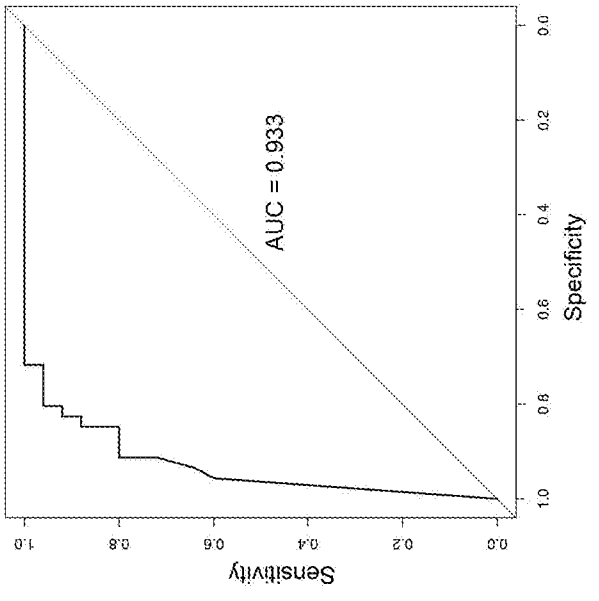


FIG. 31D

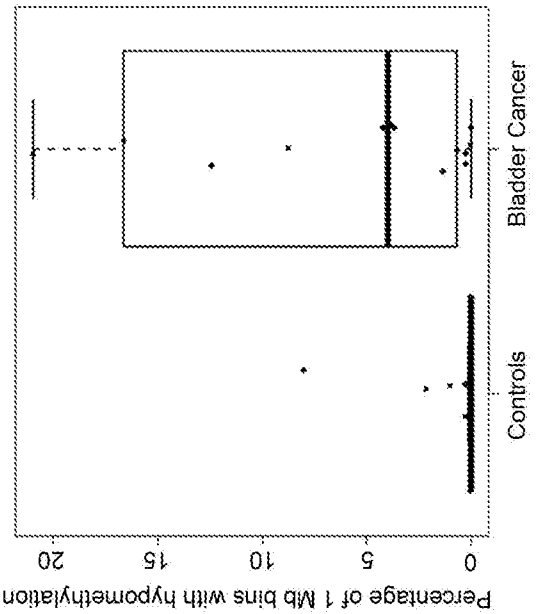


FIG. 32A

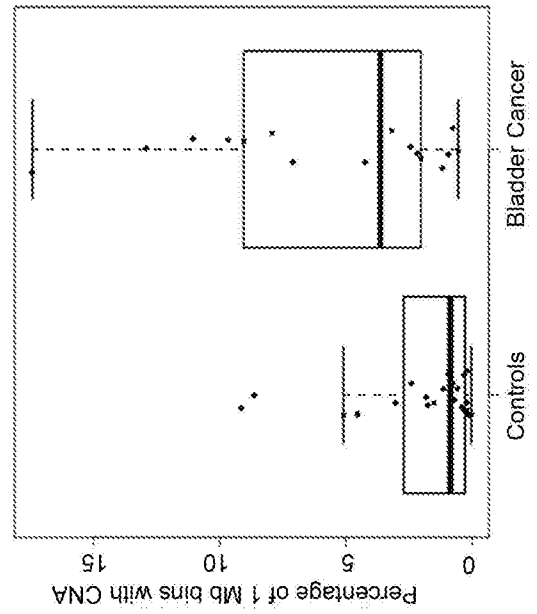


FIG. 32B

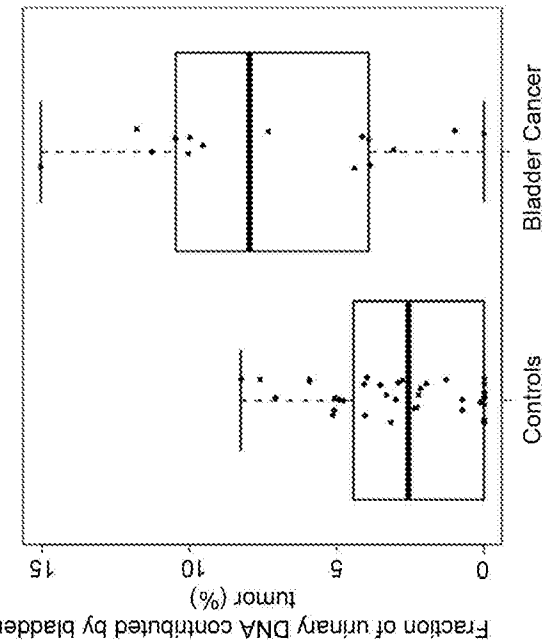


FIG. 32C

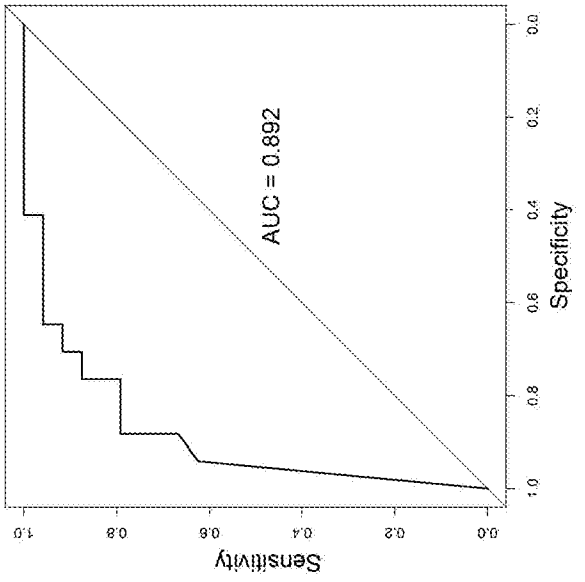


FIG. 32D

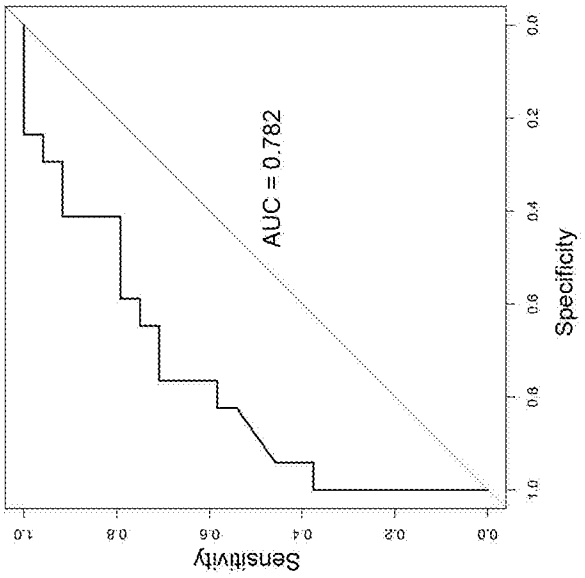


FIG. 32E

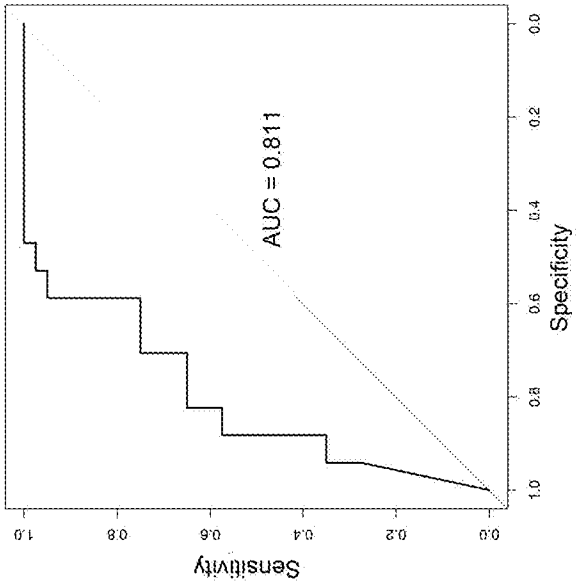


FIG. 32F

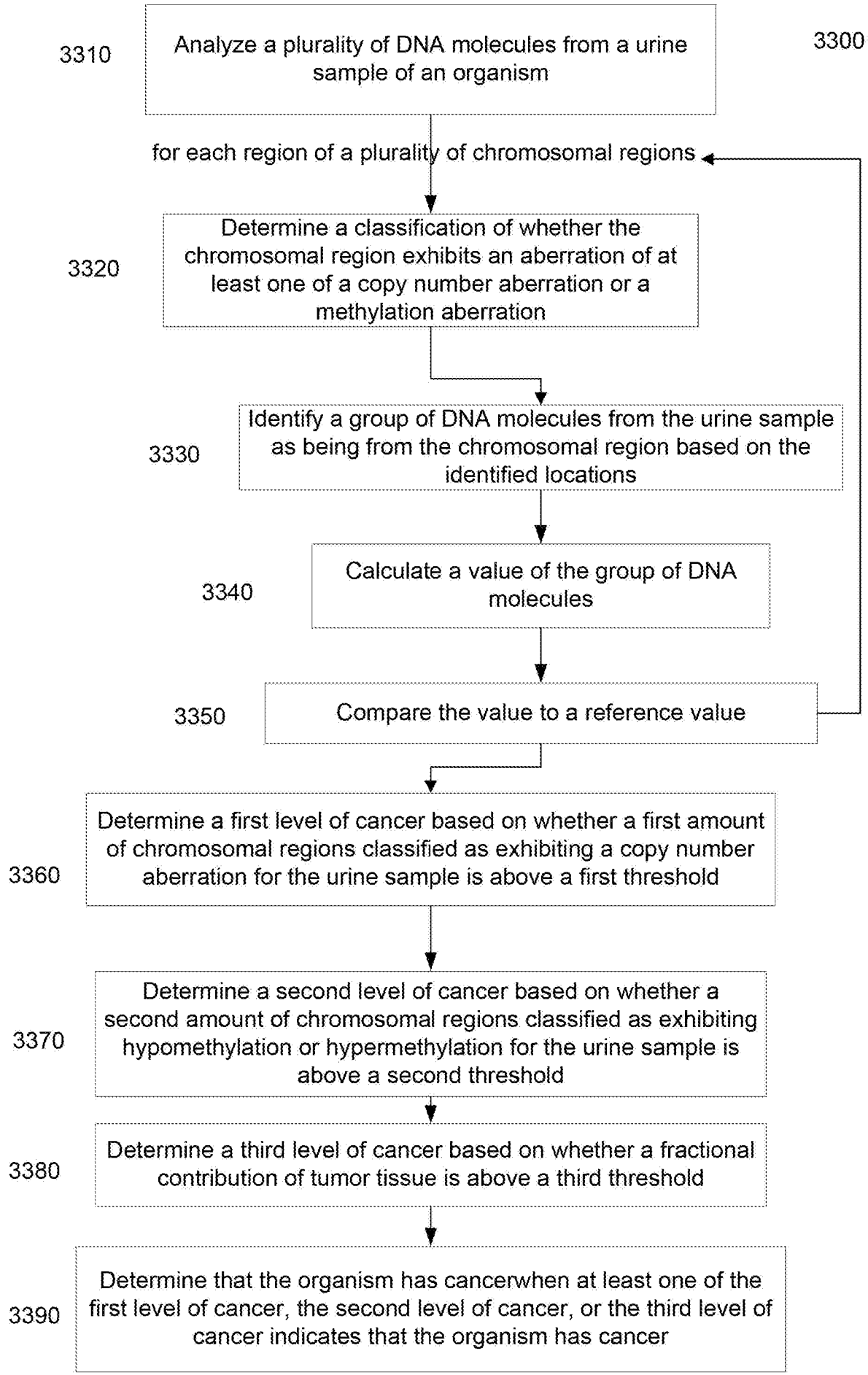

3300
3310
Analyze a plurality of DNA molecules from a urine sample of an organism
for each region of a plurality of chromosomal regions
3320
Determine a classification of whether the chromosomal region exhibits an aberration of at least one of a copy number aberration or a methylation aberration
3330
Identify a group of DNA molecules from the urine sample as being from the chromosomal region based on the identified locations
3340
Calculate a value of the group of DNA molecules
3350
Compare the value to a reference value
3360
Determine a first level of cancer based on whether a first amount of chromosomal regions classified as exhibiting a copy number aberration for the urine sample is above a first threshold
3370
Determine a second level of cancer based on whether a second amount of chromosomal regions classified as exhibiting hypomethylation or hypermethylation for the urine sample is above a second threshold
3380
Determine a third level of cancer based on whether a fractional contribution of tumor tissue is above a third threshold
3390
Determine that the organism has cancerwhen at least one of the first level of cancer, the second level of cancer, or the third level of cancer indicates that the organism has cancer

FIG. 33

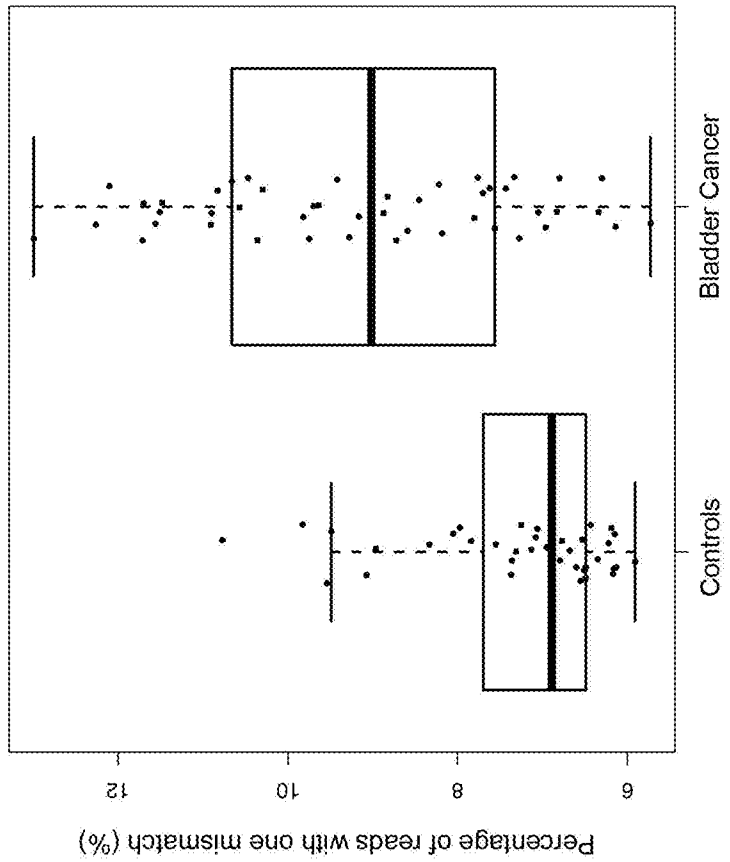


FIG. 34A

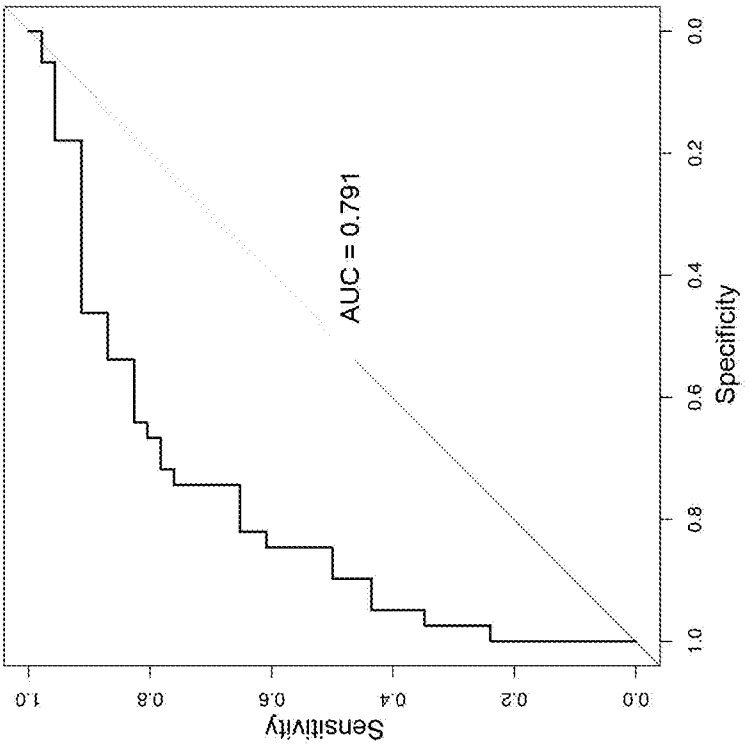


FIG. 34B

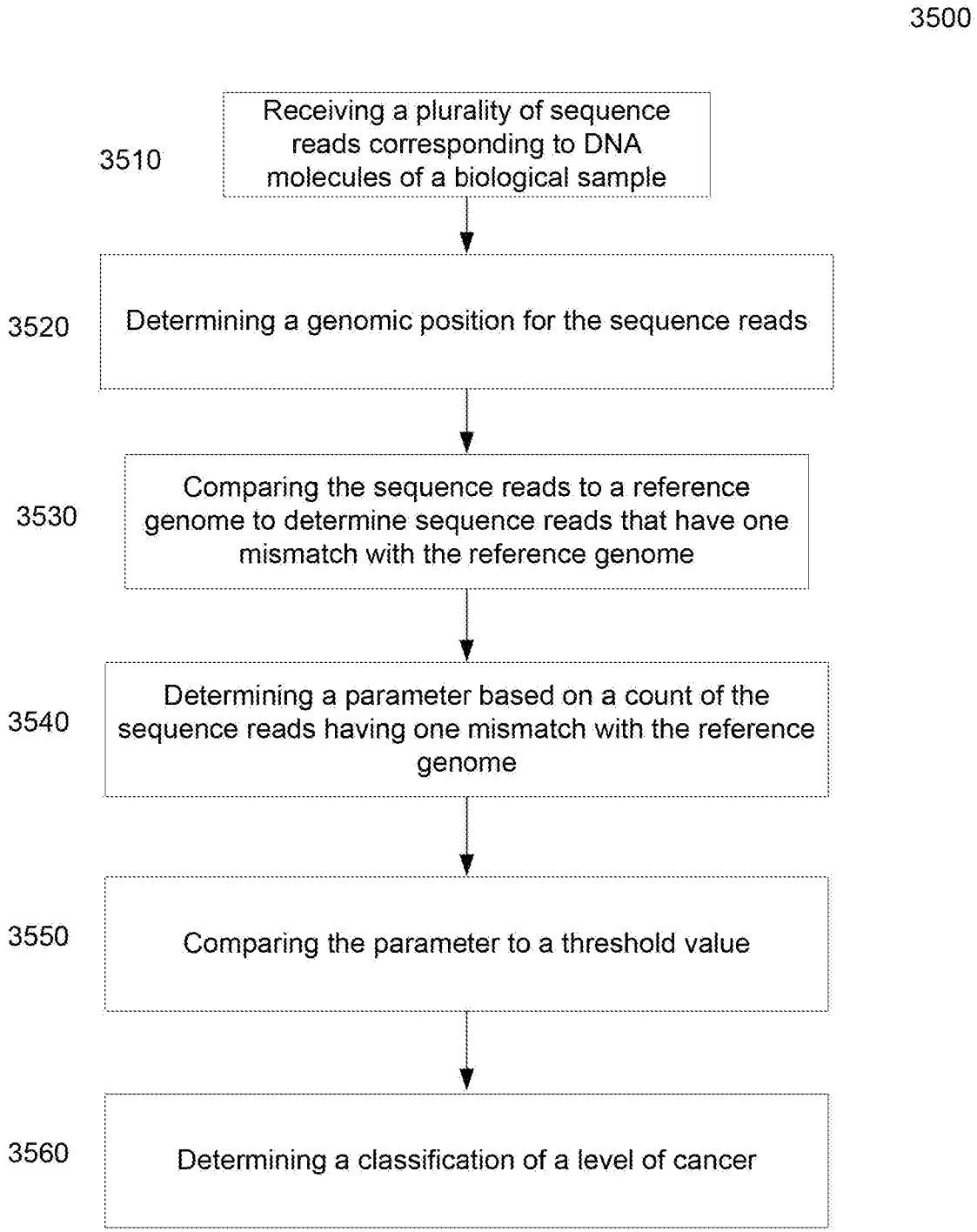

3500
3510
Receiving a plurality of sequence reads corresponding to DNA molecules of a biological sample
3520
Determining a genomic position for the sequence reads
3530
Comparing the sequence reads to a reference genome to determine sequence reads that have one mismatch with the reference genome
3540
Determining a parameter based on a count of the sequence reads having one mismatch with the reference genome
3550
Comparing the parameter to a threshold value
3560
Determining a classification of a level of cancer

FIG. 35

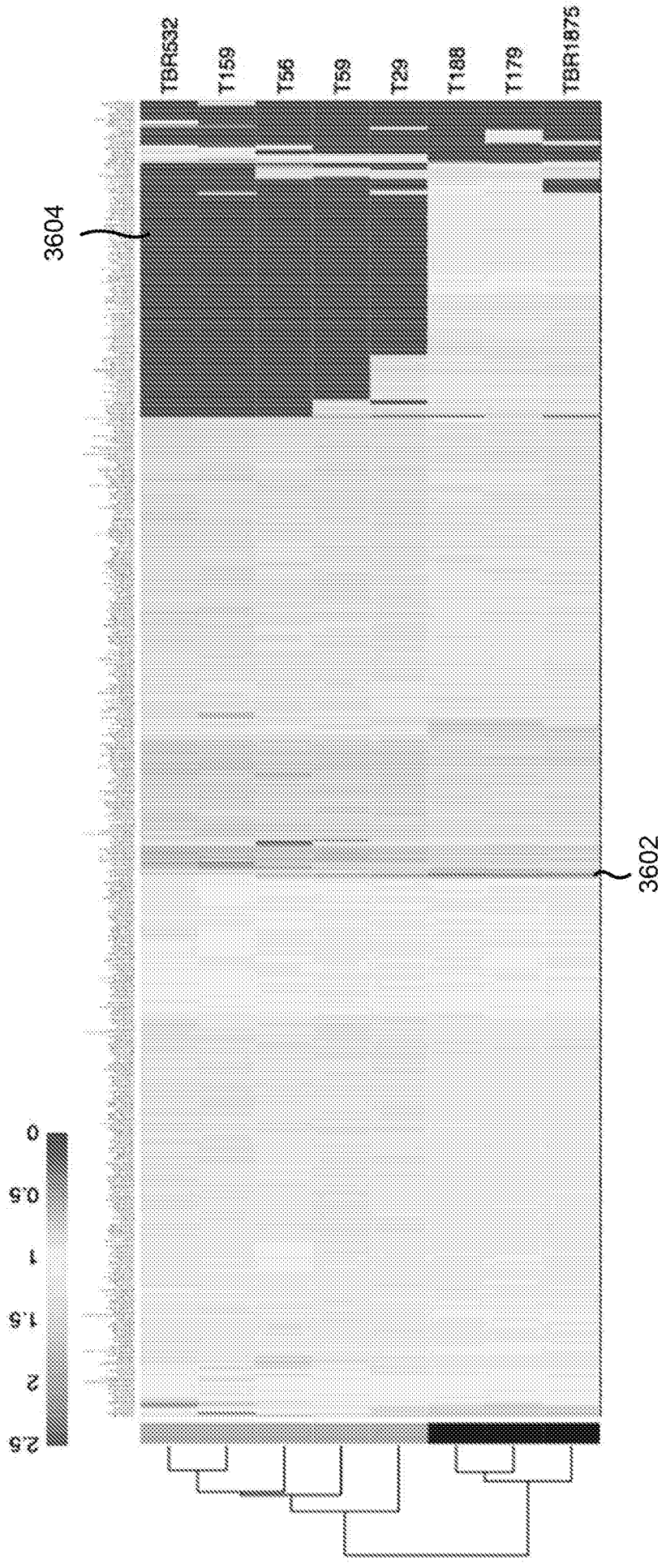

TBR532
T159
T56
T59
T29
T188
T179
TBR1875
3604
3602
2.5
2
1.5
1
0.5
0

FIG. 36

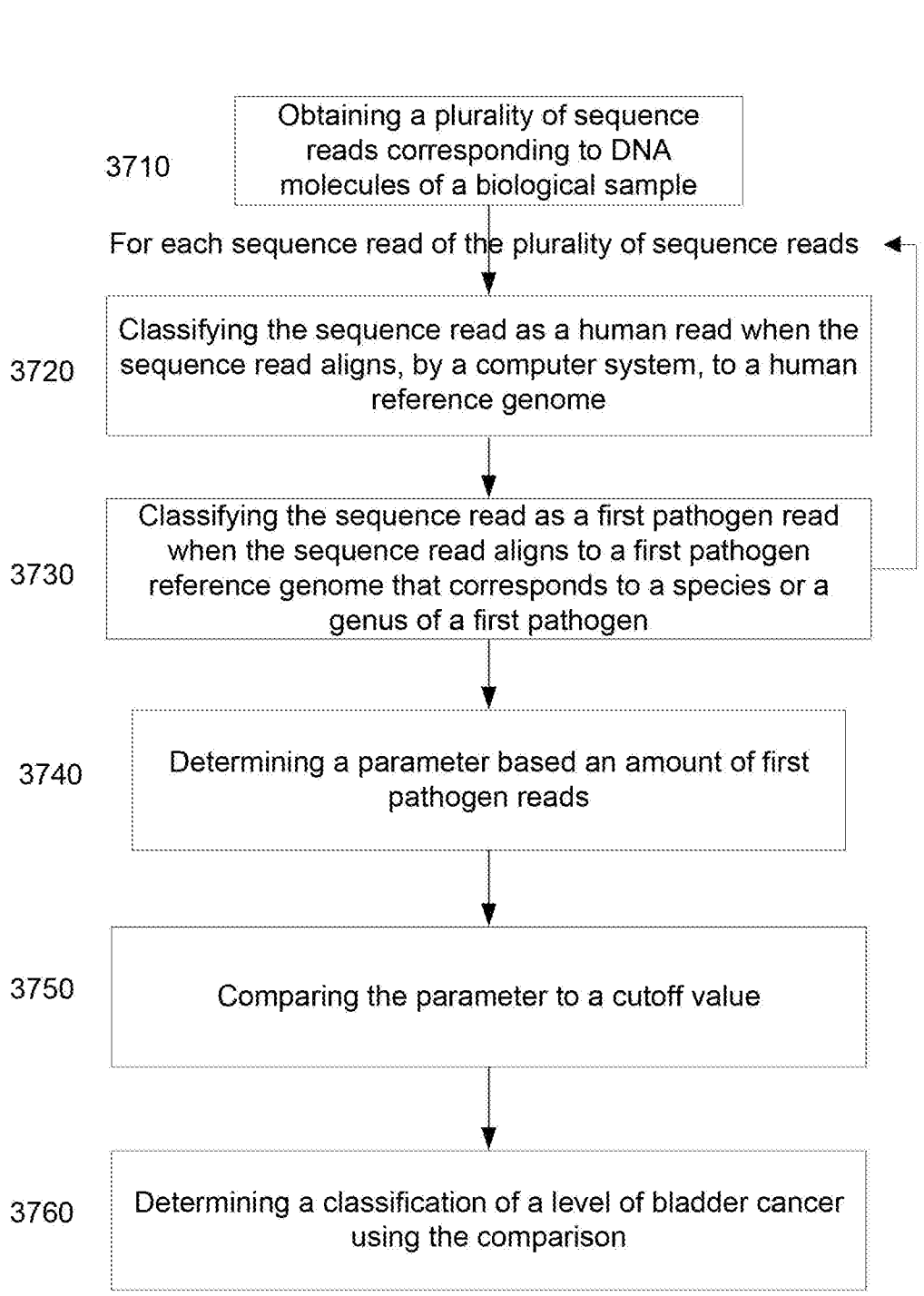

3700
3710
Obtaining a plurality of sequence reads corresponding to DNA molecules of a biological sample
For each sequence read of the plurality of sequence reads
3720
Classifying the sequence read as a human read when the sequence read aligns, by a computer system, to a human reference genome
3730
Classifying the sequence read as a first pathogen read when the sequence read aligns to a first pathogen reference genome that corresponds to a species or a genus of a first pathogen
3740
Determining a parameter based an amount of first pathogen reads
3750
Comparing the parameter to a cutoff value
3760
Determining a classification of a level of bladder cancer using the comparison

FIG. 37

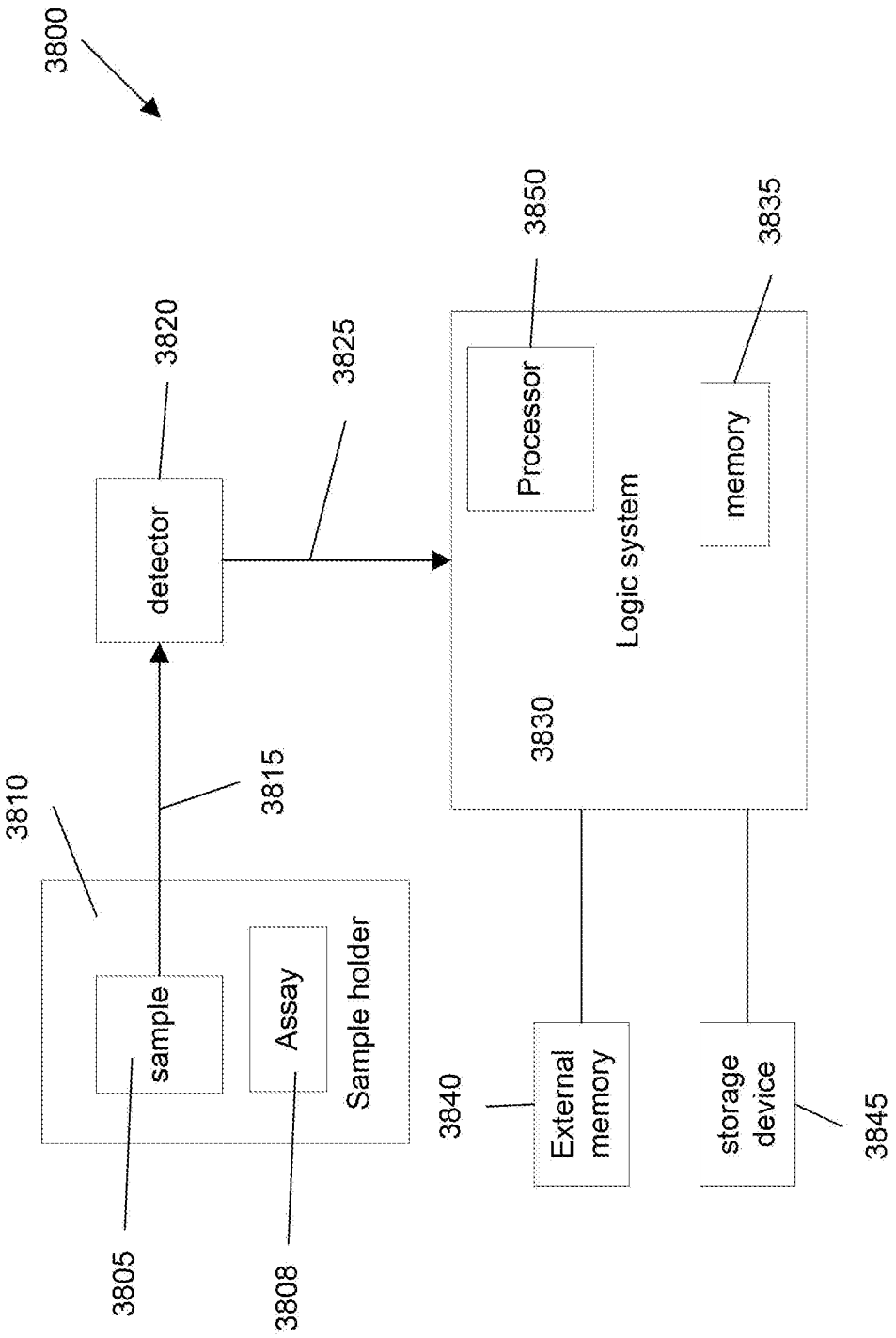

3800
3820
3825
3850
3835
detector
Processor
memory
Logic system
3830
3810
3815
sample
Assay
Sample holder
3805
3808
3840
External memory
storage device
3845

FIG. 38

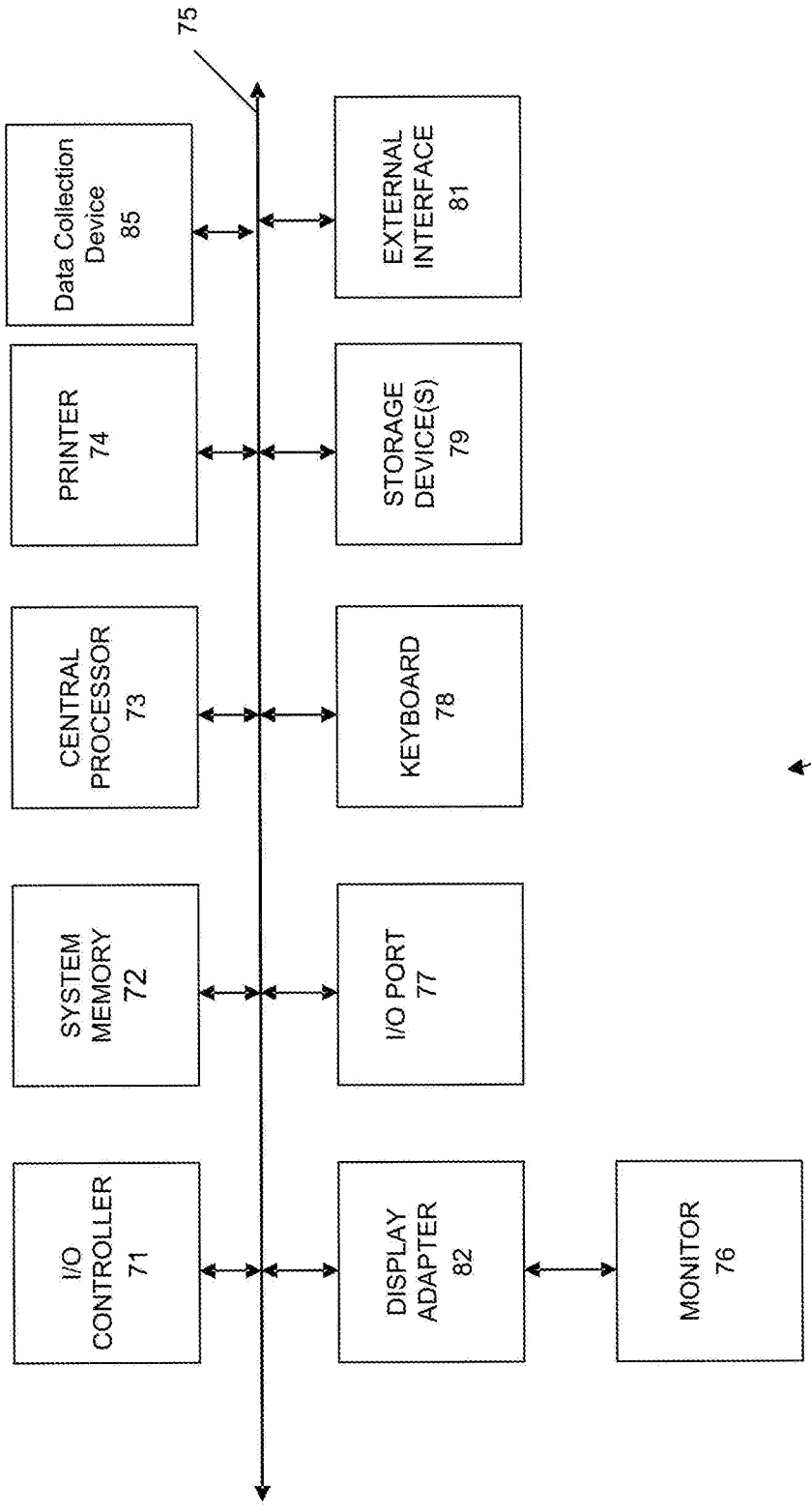

75
Data Collection Device 85
EXTERNAL INTERFACE 81
PRINTER 74
STORAGE DEVICE(S) 79
CENTRAL PROCESSOR 73
KEYBOARD 78
SYSTEM MEMORY 72
I/O PORT 77
I/O CONTROLLER 71
DISPLAY ADAPTER 82
MONITOR 76
10

FIG. 39